PAST STUDENT LEADS **CANCER BREAKTHROUGH**

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Past student and leading Peter MacCallum Cancer Centre clinician-researcher, Professor Mark Dawson's ongoing commitment to learning and innovation is 'leap frogging' our understanding of cancer; transforming prevention and treatment to save and extend lives.

Today, Mark is the Program Head for Haematology Cancer Therapeutics and also leads a group of researchers in the Cancer Epigenetics Laboratory at Peter MacCallum Cancer Centre. His research focuses on identifying new therapies for acute myeloid leukaemia (AML); a disease which holds a poor prognosis.

Mark speaks candidly about the innovation landscape, his commitment to the cause and the people along the way who have helped shape his extraordinary, meaningful career path.

"This 'Eureka' moment was punctuated by a moment of real understanding and discovery, a moment where you know you have found something very special."

Mark, it's a pleasure to meet you. I feel fortunate that the two days of the month you are in the country, you are making this interview possible, so for that, thank you.

Okay, let's talk breakthroughs and innovation and, specifically, your commitment to it. Newspaper articles are referring to this as a "double discovery" moment. Can you explain the moment this occurred and what this means to sufferers?

I guess when we hear about scientific discoveries like this, what isn't necessarily spoken about is how long those things take, and that they build continuously on work that has gone before.

From start to finish it took me just over 15 years to specialise in haemotology.

The vast majority of haemotologists see patients clinically, such as in hospitals like the Peter MacCallum or in private practice, etc., but a select few also decide to do something else, which is to try and do significant basic science research into the diseases they treat. And to do that, you almost have to train again in a very different area, as a scientist, which takes you back to doing a PhD in a basic Science field. That was the path I followed when I went to the University of Cambridge.

Along with a group of other researchers at Cambridge, one of the things I helped do was establish a new way to treat some of these cancers. The newspaper article that termed this as a "double discovery" was referring to how this drug works and how cancer cells becomes resistant to this drug. During this process, we learnt new insights into a very aggressive disease called acute myeloid leukemia. This affects about 1,000 Australians every year. The vast majority die from this condition because we don't have great treatments for this disease. What this discovery has done for us is that it has enabled us to understand this disease in far greater depth. It equips us with the tools to be able to study this disease like we've never done before. Now that we know a lot more about this disease and are able to grow some of these rare cancer stem cells, we can test new drugs in a way that we couldn't previously, and we can understand how the disease develops, enabling us to be able to find new drugs to use in new ways. This 'Eureka' moment was punctuated by a moment of real understanding and discovery, a moment where you know you have found something very special.

Wow, how incredibly satisfying.

Yes. Research is probably 99 per cent frustrating, but that one per cent is what keeps you going. I guess that if you are an amateur golfer or sportsman, take golf for example, you hit 17 holes of disaster and then on the 18th hole you drive this perfect ball… you will always come back and do it again because you remember that. And that is very much how research works. I often say this to the new students and post graduate Doctors etc. who come and train. By and large they come with me on that journey, but they also work for themselves, and that is a very special environment, because when you do discover something like this, for that brief moment in time, you're aware that you know something that nobody else in the world knows, something that will change the way we understand or do things and has profound implications for various people etc. You work very hard for those fractions of a day.

Describe to me the current Australian Medical Research Innovation landscape and its position in the global marketplace.

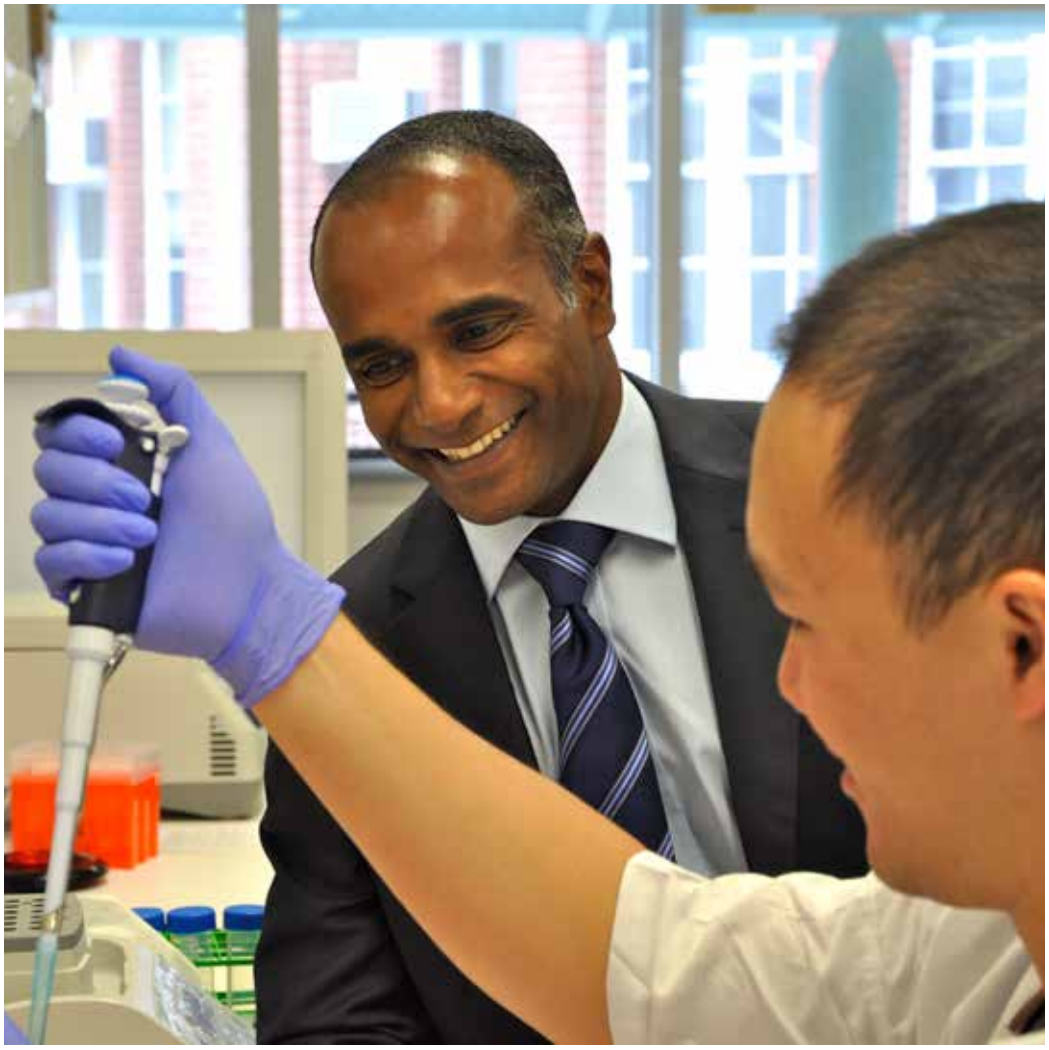
The Australian Research environment is incredibly tough, and, as a result, we have a significant brain drain in Australia. There are some exceptional Australian scientists who will never come home, just because it is far easier to achieve without the constraints of the Australian funding system. It's probably safe to say, currently, that we are in the worst funding climate that Australian science has ever seen. We have lost more people in the last year in science than ever before, people who have just simply run out of funding, and after many, many years of research aren't able to continue in their career because they are no longer able to support themselves. That's difficult, because I think that, in part, the problem lies in the way Australia values science, as opposed to exceptional endeavours in other categories, for instance, sport. We revere our sports people to an extent that we would never revere an academic. An example of this is when Elizabeth Blackburn won the Nobel Prize. She is one of very few people, and one of the first Australian women, to get one of the highest accolades in science. It was also around the time that Ian Thorpe decided that he was making his comeback. You can guess who made the front page of the newspaper, right? As a result of her Nobel Prize, Elizabeth Blackburn is now the Director of the Salk Institute, one of the best institutes in the world. She is unlikely to come back to Australia. She probably never will. Those opportunities would never have been here for her. That's a very extreme example, but it's safe to say that my wife and I, Sarah, (who also does exactly the same thing as I do – she's a breast cancer Doctor and runs a laboratory looking at and understanding breast cancer - she and I trained in Cambridge) have come back together, but we really struggled with that decision of coming back. The primary reason we returned was that we wanted to be close to our family, and, in part, we felt a commitment to try and give back to Australia. We understood there would be difficulties, but we felt we would still be able to achieve something here, but probably not to the same extent as we would have done had we stayed in England, just because our work is much better appreciated and funded in the US, Europe etc. I'd say that with Australian funding the innovation in scientific progress is appreciated, but not to the extent that it should be.

Do you see it changing?

I think it has to change if we want to be competitive in the global market. It's certainly a good start that Malcolm Turnbull is in, but it's going to need many more like him to really understand why so many people are leaving and not coming back, why they are giving their expertise to different countries. For instance, the Head of Surgery in Oxford is Australian. The Head of Medicine in Cambridge is Australian. Why are these guys not here? The same thing happens over and over again. So, I think it has to change.

You refer to high-risk high-reward research as 'blue sky research'; great analogy. How do you maintain a strong positive mindset and commitment to hope?

It's driven by different things, I think. I'd say I've always been a very ambitious person. You can run these two things in parallel. Somehow I've found over the last two decades that I can couple that ambition with compassion and a desire to look after people, which by and large is what drives one into the clinical arena, why one often becomes a Doctor. I didn't know this when I was 17 years old, or when I was going to university to study Medicine. I knew it when I was 24 years old and was about to take my first job as a Doctor. I did Medicine because I had the marks to do it. I didn't necessarily know if I was cut out for it or going to be any good at it, I just knew that it was a profession that was thought of in high esteem, and I happened to be academically gifted enough to be able to be given the opportunity to study it. I think to be good at it you need to have empathy, compassion and be able to communicate well with your patients, and you learn that about yourself along the way. By nature I am an incredibly curious person. I'm not someone who easily accepts dogma. I want to always understand why things happen, rather than just accept that is the way things happen, and that is by and large why I decided to train as a scientist. I want to know why we can't cure patients with this disease. It's not good enough to me that that is what it is, that we accept a scenario whereby only one in five patients receive a benefit from a particular type of drug. What is it about that one person that makes them respond? And what is it about the four people who did not respond, and why are they not responding and how can we change that? It's those types of questions that have driven me to science to try and understand that. So I think you have to in some way couple this curiosity and compassion and be able to drive both forward. I'm a person who strongly believes that cancer research needs to be driven primarily by curiosity. You need to be able to spot what the big discrepancies are and try to understand them. By that, I mean you need to know why it is that this happens only 'x' number of times, rather than aiming for regular incremental benefits. And so that's what



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I mean by blue sky research, because it's a very difficult question. Why is it that four people don't respond and one does? There's probably a billion reasons why this might be the case, and it won't take six months for me to discover that, it may be 15 years to make even a substantial dent in that question. You therefore need to be committed to the importance of that question, and realise that during the journey quite often you may not achieve anything because you will be going down blind alleys. Remaining focused and committed to answer the big questions is what I mean by blue sky research.

What are the research funding challenges?

I think the general public see discoveries and understand that we are getting closer to changing the natural history of some of these cancers. I guess that what the general public don't see is how long it takes. Without that ongoing support of our research from the public we won't make these fundamental discoveries. And so I think that the kind of message in the various avenues, like through the Cancer Council and other various opportunities I've had to talk about medical research, is just important to impress upon people that it takes time, because by and large this is a process that is driven by trial and error. If we already knew the answer and just needed money to get there, then it wouldn't take very long. But we are not in that situation. It is largely about trying to gain the support of people to say, well, this is difficult and we need to invest time to get there.

What influenced your desire to impart change on the world, and what is your suggestion to people out there wanting to make a difference?

If someone had showed me in 1992 what my job is today in 2016, I would scarcely have believed it. And that's because there was no great ambition to be 'person x'. I didn't have a set role model of who I wanted to be like. That evolved slowly over time, and it's influenced by a whole variety of things, mentors, people you treat, people you speak to, people you teach, etc. All along the way they help to identify things in yourself that you might not necessarily see yourself. Your strengths and your weaknesses are made apparent through these interactions. And so it is through these interactions that I understood my curious mind and ability to think laterally about questions that sometimes other people did not. That's what drove me into science. What maintains my clinical interest is that I really enjoy talking to patients. I feel that even in times of real difficulty and desperation I am able to give them some sort of comfort. But that's only been apparent by doing this for nearly 15 years. I can't see a time in my life when I won't be a clinician and see patients, because I think that in many ways I would be giving up something that I both enjoy and feel that I contribute to in a substantial way. To answer your question, what drives this? I think you are influenced by your interactions as you grow into life, and that helps hone where you end up. I don't know where I will be in 15 years. It's unlikely I will be still in the same job, and that too will be impacted by my current interactions.

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Do you ever reflect on where you are today and wonder how it came to be?

I feel very lucky. I don't ever look back on it and think, wow, I did a pretty good job of achieving it. I can quite quickly point out to you maybe five or six instances where a single thing changed where I am today. And that goes all the way back to school. I think it would be fair to say that when I was at Salesian College Chadstone, it wasn't the academic environment that some of the other schools had. I was the only one from Salesian to do Medicine at the University of Melbourne, and I barely got there, because it wasn't as though my entrance score was way off the chart or it was easy to get in, but when I got there, what I realised, was that I got there through really hard work and the ability of the teachers to get the best out of me. When I got there, I realised that out of the 200 odd people, I finished in the top 5, and that was because I was used to teaching myself, training, doing things for myself. There were two or three teachers who really pointed that out to me and were able to motivate me at the right time, at a very critical time to get me to that position. And then again at university I can say the same thing. There were two or three people who really showed me that I would be good at being a physician, and then during the time I went to Oxford, people subsequently showed me that actually, I might be a good scientist. I can very easily point out the mentors along the way who have made these major differences. When I reflect back, I also wonder what would have happened if I hadn't met those people.

Listening to and reflecting on your achievements leaves one with a strong sense of motivation to follow an authentic and altruistic cause. At what stage did you realise this was the life you wanted to lead?

None of this would have happened without my parents or my siblings. Really, they are the only people who really give you unconditional love and support. In my parents I found that in spades. They have always been, and continue to be, a major driving force for all of this. So I think that, above all, they would probably be the best mentors. There were also a couple of key teachers at school. Teachers in many ways are meant to be very impartial, but I think that the good ones often identify people who they know when to push. I had always been this person who was academically capable enough to coast, and never really pressed myself enough to stand out. Part of that was probably that mindset of never wanting to stand out in any set ways at school. It's always better to be part of the crowd. But there were teachers who really identified the fact that I really wasn't pushing myself and motivated me to do so. And that really happened late in the piece, but at the exact right time when it needed to happen.

Do you remember who those teachers were?

Yes, quite clearly, actually. John Nolan and Patricia Burns. Both of them really understood who I was and were able to get the best out of me. At university there were others. Probably the person who showed me that I was likely to be good at science was a guy called Bill Robbinson. He was an American who happened to be in Australia at the right time to do science, and he was a fantastic mentor. He really changed the way I thought about Medicine and Science and showed me that you could do both very well. Later in the piece, the most important support and ongoing inspiration is my own family now. My wife, with whom I work and see 24/7 – we share an office, we run two separate laboratories that are co-located, we do very similar jobs and we have two children. We've never really worked together before, and have only done so in the last 18 months, but, you know, she completely understands the pressures we have, as she has the same. She understands the ambition and the drive, because she has the same. And so it's easier to do what seems like a difficult job when you're with someone who knows what that's like.

It's clear that teachers John and Patricia had a lasting impression on you – why else do you look back so positively?

Certainly the teachers and their ability to understand and motivate, but also the friendships I had. It was a very diverse group of friends that I had and whom I still meet with today. We have taken completely different career and life paths but I think when you spend six years together at an all-boys school, you have the ability to form this incredibly tight mateship, that potentially lasts an eternity. Some of these people I have not seen for 10/15 years, but when I catch up with them, it is as I have always known. I think the fundamental core of who we are doesn't really change, and so I'm also very grateful for that, for those sorts of friendships. I don't take them lightly because I don't think they happen very often. It is the training to be independent and resourceful which are the kinds of things I learnt at Salesian.

You have 15 years of research experience, Mark. What are the critical factors when talking successful innovation?

I think there are a couple of things. Firstly, you have to be fearless. You can't be constrained by what you think is possible. If you think this is not possible to do, to answer, to explore, then you will never do it. History has taught us that the greatest advances have come when curiosity has pushed back the boundaries of the impossible. So you have to be fearless and you have to focus on what the agenda is, not necessarily what the tools are to get you to that agenda. If the tools aren't there, build new tools. So I think that's one thing. You also have to be open minded. By that I mean that there are people who question every single matter of life. I don't think that's very productive, because there are some things that are just clearly, simply true. One plus one will always equal two. You also don't want to accept everything as fact. You need to find a way of balancing that and knowing how to use that to tease apart what we know and what we need to know. You have to be patient, which is something that comes very difficult to me. I'm not a very patient person, but I've learnt you have to be. You can't expect results to turn up every day. If you do, you're setting yourself up for disappointment.

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Surely that must be an ongoing challenge every day for you, is it?

Yes, absolutely. By nature, I'm not a patient person (I don't think many ambitious people are), but you have to learn to be patient and tolerant. Those are the things that make you at least open to the possibilities that a positive outcome will happen.

What does good leadership look like to you?

I think what makes people good leaders is clear focus and direction, but that's only useful if people come with you. You're not leading if you're the only one walking in that direction. Therefore, to get people to come with you, you need to be able to convey that vision and inspire others to see why that is worthwhile achieving. That requires the ability to communicate, and that communication has to be pitched at the right level, so you need to take the time to understand who it is you're dealing with. There are some people who are already working at capacity, but may need some direction to achieve much more. There are some people who are not working at capacity who can achieve a lot more. They are ones you need to push, and then there are those who you need to congratulate for what they are doing and not necessarily move them in either direction. It's understanding those subtle differences that makes good leaders.

It's not only in working, but in daily life. Your kids teach you some of this. I have two children, and their personalities are diametrically opposed, but along the way you learn how to get the best out of both of them.

Are you a man of faith?

It's an interesting question. I will always be a man of faith, but what faith is to me now is very different from what it was when I was starting school in 87' and finishing school in 92'. In part, I do a job that challenges the existence of God all the time. But I've managed to find an area where this dichotomy exists pretty peacefully for me. It's very hard to describe how you reach this equilibrium where you do not have to choose between two opposing views, "there is no God" and only science can explain all natural phenomenon, as opposed to blind faith, whereby you believe everything that happens every day is driven by God's will. So I sit at neither end of that spectrum, and have found a comfortable seat somewhere in the middle, but it is very difficult to describe in words what that comfortable seat is or how I managed to find it. The Catholic faith is still fundamentally an important aspect of my everyday life. My two kids go to Catholic schools, and we chose very specifically for that to happen. We still go to church, and in many ways I find sometimes the greatest comfort when I'm by myself, saying a prayer. It's a difficult thing to explain to people if they have never had that opportunity to be exposed to that environment early in life. You become comfortable with accepting that there are things that can be explained, and things that can't. There is definitely something greater than just us.

Mark, you're a busy man; a genuine thank you for your time. Please continue along this incredible path you lead, and on behalf of many, thank you for your commitment to the cause.