SNOWDOME Q&A SESSION WITH RESEARCHERS

For the benefit of our passionate partners and supporters, Snowdome recently held Q&A sessions with some of the brightest young Australian medical researchers who are dedicated to finding new treatments for blood cancers. The following is a summary of the interactive Q&A session held on 31 May 2016 and features researchers closely aligned to Snowdome.

Host: Professor Miles Prince (MP), co-founder of Snowdome Foundation, who posed the questions to the various members on the panel.

Panelists' bios are found at the end of the feature.

1. **MP: Ricky, why did you choose to be a researcher?**

Professor Ricky Johnstone: I'm different to others on the panel in that I don't have a medical degree. I'm a scientist – trained + PhD at University of Melbourne then Harvard University to do post-doc fellowship where I got involved in cancer research. I'm attracted to the thrill of discovery and come to work every day thinking "we're going to discover something really important today". As my career progressed I've seen ideas translate from the laboratory to the clinic in a much quicker time frame. It used to be 5 years but it's now 5 days. We understand the genome like we've never understood it before. We've got advanced technology that we've never seen before and that we can tap into. I love collaborating with my clinical colleagues over discoveries to ultimately make a difference. Jake Shortt did a PhD with me in the lab and it was really interesting having a clinician in the lab to get his perspective so we could really focus our ideas to try and ensure the research was translational.

2. **MP: Jake, we hear the word 'genome' used a lot, what does it mean?**

Associate Professor Jake Shortt: Genome describes all of the genes in the person's body, but in our context it's all the genes that are in the blood cancer or the cancer and, in particular, how they differ. If you understand how the genes in the tumour differ from the genes in the person then you have a roadmap for identifying vulnerabilities in the tumour that you can then target with the drugs you have available. When I did my PhD with Ricky, which started in 2008, we didn't have any idea about the genomes that we were dealing with. With the advances in technology, we can now test and identify genomic diagnoses within 2-3 days. The understanding of the genome has really revolutionised our understanding of the cancers but also our ability to bring effective therapies to the clinic.

3. **MP: If I am a patient with lymphoma presenting to you, tell us how you approach the concept of genomic testing?**

Associate Professor Jake Shortt: The technology is readily available in a research setting but it's transiting to the clinic so at the moment I would have the discussion with patients whose lymphoma isn't behaving the way we'd want it to or wasn't responding well to therapy. I'd suggest that if the conventional treatment wasn't working, then knowing more about what's underpinning their particular lymphoma and what makes it different from the other lymphomas that are responding appropriately so we can think of more innovative ways to treat it or preferentially allocate someone to a clinical trial that aligns with the particular biology of the lymphoma. It's a very difficult discussion to have with someone who perhaps hasn't heard the word 'genome' before or doesn't know a lot about lymphoma and I think that's one of the complexities when you start delving into the tumour genome and the person's genome because it can have implications for the patient and their family members. I'm still learning how to have that conversation and it's different every time.

4. **MP: The assessment of genomic work has only become available in the last year or so as a standard treatment. Piers, tell us how you fit into that?**

Dr. Piers Blombery: I'm the lead of molecular pathology and haematology at Peter Mac. I take these research technologies we're talking about – next generation sequencing – the ability to look at hundreds of genes simultaneously and try and somehow bring that in to a quality controlled, accredited environment that's a fit-for-purpose investigation for treatment for patients. So, the research sphere is governed by a certain amount of veracity of process whereas the pathology sphere, when we're making tests to guide patient's treatment, we have to have a level of quality assurance that the result we're providing is correct all the time, every time. So, that's basically my job and I'm trying to transition these technologies in a controlled way for patient care. We've started off dipping our toe in the water by looking at just 20 or 25 genes initially (there's about 20,000 coding genes in the genome, of those about 300-400 are of interest to cancer). The 20 to 25 genes

we are looking at are the high tier, really actionable, meaningful genes today. These are the genes you can target with drugs, they're the ones that can change diagnoses, that change patient's treatment.

5. **MP: An example? What happens day to day, how your results have impacted?**

Dr. Piers Blombery: We run these tests all day, every day. We find mutations in a patient's genome that might drives leukaemia and there are currently trials running around Victoria which targets that particular mutation so we can recommend that targeted treatment and the patient often has a favourable outcome compared to conventional therapy. We overturn diagnoses for patients who are often treated for a particular diagnosis but because they are not reacting appropriately to treatment we run some tests. We find a mutation profile that actually suggests they didn't have the disease they were treated for to begin with. There are hundreds of thousands of anecdotes I could give you about the changes we've made just with these 20 or 25 genes we've been looking at.

I guess the next step is moving from these 20 high-priority, top-tier genes to a really personalised approach where we're looking at 200-300 genes plus the expression of these genes. What are these genes doing inside the cell? So that's the next challenge in bringing that technology into the accredited sphere.

6. **MP: Piers, how does this genomic work compare to Europe or America?**

Dr. Piers Blombery: The service we provide at Peter Mac is, not to my knowledge, available anywhere else in Australia. And I have come from the UK where the molecular service wasn't as good as what's happening in Australia now. I think that's because we're the right mixture of being small enough that we can 'bespoke' the care for our patients. I think what we're doing in Australia is world class.

7. **MP: Sharon, you're one of the most senior clinicians and researchers working in this area – where do you think Australia sits in the world in terms of its research capacities?**

Professor Sharon Lewin: I'm a clinician scientist and I'm passionate about translational science which means taking what you find in the clinic to the lab and vice versa. I'm an infectious diseases physician and I've always worked in HIV which is an unbelievable story of being a universal death sentence in 1981 to a chronic management disease with normal life expectancy in 2016. I'm very much driven by science – that if you invest heavily, the results will come.

I was in New York in the mid-90s at the very beginning of anti-viral therapies and worked with a man who was making many discoveries. So it was a very exciting place to be. I still think that international postings are really important in science, to broaden our researcher's experience, learnings and networks which they can then bring back to Australia and then access that network to trial drugs etc.

The research that Snowdome invests in is internationally competitive.

8. **MP: Michael, can you tell us what you do on a day to day basis and how do you choose new Dr.ugs to develop?**

Dr. Michael Dickinson: I'm a clinician and haematologist and see patients more than work in a laboratory. My research interest is executed through the conduct of clinical trials, looking at new drugs. My relationship started with Snowdome a couple of years ago when I was granted an epigenetics fellowship to develop a particular group or class of agents that target cancer development in a certain way (HIV as it happens). Ricky's lab works in that field and has led that field in many ways. During that fellowship I got my higher degree which was mostly through doing early phase clinical trials of drugs that were otherwise not available to patients in Australia and looking at either improving cancer outcomes or finding new treatments and developing new treatments or looking at using established treatments in a more targeted way or reducing the side effects from those treatments. And some of that work was then expanded into multi-national studies which I went on to lead, eg. a study that was in 43 countries and 170 centres so that's been a really exciting development for me and developing my skills and bringing these treatments to our patients. I then moved on into this new role which is really as a strategic enabler trying to bridge that work between clinical trials, what's happening in the research laboratories at Peter Mac and then infrastructure building to look at this work that Piers is doing to bring genetic testing to the clinic in a way that is broadly applicable to all the patients that we see. In the beginning focus on myeloma and lymphoma and enables us in the short term turnaround identify which of these new drugs that we work on are best applied to which patients. So I focus more on clinical treatment but that 'glue' between the research lab, the genomic testing and the clinic is something that I think we excel in at Peter Mac and the VCCC and that's really been what my input has been – to try to develop that infrastructure. Piers runs a team of 6, I have an additional 3 staff largely supported through philanthropic support (Snowdome) and that has really enabled us to grasp this moment and participate at a time when we can lead and that's been crucial.

9. **MP: Carrie, you're the Snowdome Epigenetics fellow. Tell us about where you are in your career. You've seen people, like Michael, who are 4-5 years ahead. What interests you about getting into this area?**

Dr. Carrie van der Weyden: So, I'm probably more of an accidental researcher than some of the other people on the panel. I finished my haematology training at the end of 2014 and was looking around for what to do next. The big question was 'do you just want to go out and treat patients and look after patients or do you want to do something else, maybe take a bit of time out and study something in a bit more depth'. That's what I opted for and ended up at Peter Mac working quite closely with Miles and Michael. The exciting thing for me is the capacity to see what a real difference we are actually making to patients in the clinic. So one of the clinics that I do is looking at patients with a very rare type of lymphoma, a skin lymphoma. It's not something I'd looked after prior to

coming to Melbourne in any meaningful way but looking after that cohort of patients and looking at their participation in clinical trials gives you the capacity to realise how vital that research is to delivering meaningful care to groups of patients who would otherwise miss out. And I guess moving from that small anecdotal experience you can then begin to understand how that paradigm can start to translate to other groups of patients. So it's quite an exciting place for me to work in and to see exactly how real and meaningful research can be at the coal face.

10. **MP: So talking about meaningful research … Mary Ann, you've been working with probably one of the most exciting drugs in the world which started off in Australia in the laboratories here. Tell us about the history of that drug and how it fits into your life.**

Dr. Mary Ann Anderson: I work with a drug called Venetoclax which targets cells to commit suicide. So, we know that a protein is over-expressed in cancer cells that's not expressed in normal cells or at much lower levels of expression. And by using this drug we can turn that protein off and cause the cancer cells to selectively die. What is really exciting about this story is that this abnormal protein, BCL2, was first described back in Australia in 1988 at the WEHI where I work. Over the last 30 years, research in Australia and overseas has really developed the BCL2 story so that we now understand how it is that BCL functions and how it is that it can contribute to the growth of cancer and also understand its resistance to chemotherapy. Over the last 10 years we've started to develop inhibitors of BCL2 and some of the earlier drugs where either not effective of associated with intolerable side effects. And I started my PhD in 2011, when we started a clinical trial with this drug Venetoclax, which was the new BCL2 inhibitor, so it was designed specifically with our knowledge of BCL2 to target it but not other proteins, so we could hopefully turn off the driver of the cancer without causing side effects in our patients. And we gave this drug to the first person in the world in 2011. This person had failed multiple lines of therapy and this was really his last option. He came to us with a tumour the size of a football under his arm. Within a week, it had reduced to the size of a tennis ball and within a month it was the size of a golf ball. Quite quickly we were unable to feel the lump at all. Subsequently, we've gone on to treat 160 patients on the phase 1 clinical trial. Overall, 80% of patients with CLL (chronic lymphocytic leukaemia) have responded to this drug and 20% actually completely respond so there is no evidence of cancer. We're now using the drug in phase 2 clinical trials and moving into phase 3 trials in combination with standard chemotherapy and targeting the drug to patients in whom we know responses to traditional chemotherapy are not very good and that's where my work ties in with Piers. We know that people who lose their P53 protein don't respond very well to standard chemotherapy for CLL so Piers quite often tests my patients to see if they have mutations in this gene and if they do then we know that Venetoclax is actually a really good drug for them. So, there's a whole lot of questions going forward and work to be done but for me it's a really inspirational story about what can be achieved internationally and here in Australia to try and tangibly change the lives of our patients.

Mary Ann Anderson (Gandel Philanthropy and Snowdome Innovation Fellow) and Helen Gandel, Snowdome Director.

11. MP: Ricky, tell us more about your research because you work a lot with mice.

Professor Ricky Johnstone: Yes, mice are my patients. So Piers mentioned a gene called IDH2 that we've now discovered is mutated in AML (acute myeloid leukaemia) so we want to work out how to best use the drugs that can now target this mutant form of the gene. Can we model resistance? because that's a major problem clinically. These are the sorts of things that Jake brought to the table when he came to the lab, ie. you've got to think about resistance, we've got to be ahead of the game. So what we do is use mice to model the exact genetic mutations that occur in patients. We put those mutations into mice and develop the disease and treat the mice like patients and looks to see if resistance will occur and how we can overcome it. So now we're working hand in glove with what's happening in the clinic and what Piers, Jake and Mary Ann are talking about. So we're now trying to get ahead of the game and predict what might happen in the clinical setting using our mouse models. And that's really powerful because if gives us options down the track – if a patient relapses using one of these targeted therapies, what options may be available, what does the pre-clinical testing tell us and the reason we can do that is we accurately reflect the genetics of the human disease in our experimental mouse models and this wasn't feasible years ago but now we can do it. So, you talk about personalised medicine and that's true from the patient's perspective, but this is personalised laboratory medicine because we are reflecting the genetics in the human state into the mice.

12. MP: So, this is all well and good, what do the Americans think of us?

Professor Ricky Johnstone: We compete on an international stage and we want to be the best in the world. That's how we peg ourselves, just like Sharon does with her institution just like all the institutions in Australia, that's how we have to think. But the best way to do it is to work collaboratively with our colleagues o/seas. So every person around this table would have major collaborations with the U.S. and Europe and that's the only way to go. Here in Australia we are innovative and we are a bit more nimble, we have to be smart about what we do but we have to work with our colleagues in the U.S. and that's what we do. This IDH2 project is an example where

we're working with pharma and academic institutions in the U.S. on this particular project. So, you're in the game. If you're in the tent and you understand what's happening, then I think you can be competitive. If you're outside it, and trying to just work away down in Melbourne then I think you're a dead duck. So we have to put ourselves at that world stage and we have to be able to work with our international colleagues and add some value and that's why we need research excellence and that's where the bar has to be set. That's what Sharon said. It's what we do at Peter Mac, it's what they do at Monash, at the Walter & Eliza Hall Institute (WEHI), and its becoming a sort of a minimum standard that we're setting in the country.

13. **MP: So Jake, tell us about the Monash facility that you run.**

Associate Professor Jake Shortt: Monash has just commissioned a new translational research facility. It's an $84 million building, 6 floors, one floor is entirely dedicated to clinical trials. It's like a ward of the hospital except it's only for clinical trials patients. I'm responsible for a sub-set of that in the haematology setting. It's a general hospital so there are trials in other disease areas. The facility also has genomics platforms that can do the testing that Piers does at Peter Mac including basic research labs with a floor dedicated to cancer. It's been a real boost to our service out in the south-east and provides opportunities for cancer patients in that catchment area.

14. **MP: How do you attract big pharma to come and do those trials?**

Associate Professor Jake Shortt: It's actually quite easy at Monash because the geography of the place means we're in a large patient catchment, in excess of 1.3 million people. For trials in rare diseases, accrual can be difficult even where there's an unmet need, so it's attractive for pharma to work in a place where you have the capacity to recruit large numbers of patients for the clinical trials, especially now with the new facility.

15. **MP: Mike, you're doing similar things, why do pharma come and do trials with you. Do you find it hard or easy, what are the things that make it happen?**

Dr. Michael Dickinson: As Jake said, a key factor is the ability to recruit patients. We're entering an era of precision medicine, so the ability to find the right drug for the right patient based on tests that we're now doing routinely in the laboratory. So one of the things that's attractive to pharma is that integrated relationship between the research and the pathology lab and then a safe, properly regulated, highly trained clinical trials environment with expert trial clinicians who can look after patients in the way that clinical trials demand. I think that another aspect is the relationships between the clinicians and industry – track record, prior publications, seeing each other at international meetings, regular discussions early in the development phase – if you're "in the tent" or at the table and understand the translational considerations, understand the genomic considerations, have a strategic direction for the trials program, with a high quality service then you get invited to the discussions about 'hey, we've got this new drug and how should we use it?' It's a

team job and different people bring different skills 'into the tent' and that ability to connect across that skill set is what attracts industry. They see a cohesive approach to drug development.

16. **MP: Carrie, you're at the start of your higher degree, what do you see as the big issues in blood cancers that we have to address?**

Dr. Carrie van der Weyden: I think Michael's touched on this but I think it's about understanding how we personalise medicine, how we personalise treatments for our patients which coincides with our understanding of the genome. And I think we're moving from the sledgehammer approach of treating blood cancers (one treatment for all patients). The paradigm now is shifting and I think it's very much more about understanding the driving factors that cause the cancer to exist and what causes it to react or not react to different treatments. That evolving understanding of how cancers behave and how they evolve is going to fit very nicely into being able to select personalised treatments for patients.

17. **MP: Mary Ann, you've talked about killing cells or teaching them to commit suicide. Is chemotherapy gone?**

Dr. Mary Ann Anderson: I think that chemotherapy is still going to have a role in certain diseases and for certain people but ideally as technology evolves we'll be moving to an era where we can use targeted therapies where the specific mutations in a specific person's cancer so that the cancer cells die while hopefully preserving normal cells. And that offers our patients new hope in terms of potentially more effective treatments but it also hopefully means that the side effects of chemotherapy will become less.

18. **MP: Sharon, you're an immune expert, is the immune system important?**

Professor Sharon Lewin: It's important for everything but I think it is unbelievably so in cancer. So my background is in infection and immunology and of course HIV is a major infection that destroys the immune system and that's my interest but over the last few decades there's been this revolution in understanding that the immune system's critical for getting rid of cancer. We knew that for a long time in skin cancer but now it's becoming apparent it's more relevant in other cancers. In the last 5 years there's been these new drugs that basically give a kick-start to the immune system and they're now licensed. In fact Australia and Melbourne (Peter Mac, particularly melanoma) played a really big role in getting these drugs licensed. In fact Ron Walker made it really very visible and these drugs are very relevant to HIV, in fact I call it the Ron Walker drug. It's a great example of patient advocacy, Ron Walker got behind these drugs and they're now licenced in Australia and available to anyone with the right sort of melanoma and now going to be available for other cancers. So, understanding the role of the immune system and cancer is really going to change the outlook and also I'm very passionate about taking lessons from other areas and applying them because it's that intersection across different disciplines that you get major breakthroughs and these drugs are actually now being investigated in certain chronic viral infectious diseases because viruses persist at the same rate

cancers persist so you can basically boost the immune system to get rid of the virus and the cancer. So it's a very exciting new area that we're now seeing unfold.

19. **MP: So it must be tricky because an overactive or underactive immune system can cause all sorts of other problems, could this all sort of blow up in our faces and go wrong?**

Professor Sharon Lewin: It is certainly a fine balance and we've got these drugs I'm talking about called immune checkpoint markers or blockers because there are all these checkpoints that we naturally regulate our immune system to not be over-active or under-active. And it's when those go wrong that we start getting disease. So the first example of an immune checkpoint blocker actually has a lot of side effects causing the immune system to go a bit crazy and give you this, what we call, auto-immune disease. The new drugs have got less so I think we're going to refine that. Snowdome is very focused on translational research, clinical trials for patients which fills an amazing need because it is quite difficult to get funding for those areas of research which has direct benefits for patients.

Dr. Michael Dickinson: I'd like to add something to that Miles. I think that there is a question about 'are we going to get rid of chemotherapy?' and we've talked a little about international links and the P1 inhibitors are about to really explode in haematology and they will be very active with some of our blood cancers either alone or in combination. With the support of organisations like Snowdome we're able to propose trials that break out of the development idea, work with international groups and come up with something a little different. For example, a proposal that we're working on at the moment is taking one of the P1 inhibitors and giving it to some patients who are unfit for chemotherapy in the frontline setting. And it's a collaboration with an Italian research group and if we're successful with this proposal we're going to run it off our own bat and try and address the question about removing chemo altogether for some patients. It's an important question for our older patients.

20. **MP: Mary Ann, you've just talked about your drugs combining so you'll have a million ideas I'm sure about how to use this drug, in various combinations and different treatment patient groups?**

Dr. Mary Ann Anderson: It's an exciting time because we know that the drug Venetoclax works and we know that it's safe. So the next question is 'how do we utilise this drug for the most appropriate patients?'' Already we've started a trial for patients who have a mutation or a deletion in one of the very important tumour suppressor genes (P53). By targeting those patients who've had a poor response to chemo, both upfront and in the relapse setting, with single agent Venetoclax, we're seeing responses. For me, finding the patients to target these new treatments is important. We're also running studies in lymphoma to combine Venetoclax and chemo to check responses. We've got another study where we're combining it with an immune agent called Rituximab and the combination of the two seems to be slightly more effective. In the future we want to even more specifically target tumours that we know have mutations in the relevant genes. So there is a very aggressive form of lymphoma called the double hit lymphoma in which patients over-express BCL2

but also MIC and in the first instance we're hoping to combine Venetoclax with chemo in these patients but going forward, with the development of MIC inhibitors, also adding these inhibitors to the equation.

21. MP: So, who will write these trials? Do you do it?

Dr. Mary Ann Anderson: Yes, myself and my collaborators, other members of the team - we propose these trials using our knowledge from the laboratory. We seek funding for them in the first instance from drug companies or philanthropic institutions. Unfortunately, government funding for great ideas is limited. There are lots of people who have great ideas and it's a very competitive process and I think that anyone who's worked in research can tell you of the hours they've spent applying for funding and particularly with government bodies, such as the National Health and Medical Research Council (NHMRC), the success rate of getting funding is very, very low.

22. MP: So, Jake, why don't you invent a new drug, patent it and make millions?

Associate Professor Jake Shortt: Because we're probably too focused on doing trials and seeing patients and doing the research but within that I certainly don't have a medicinal chemistry focus although we collaborate very closely with the medicinal chemists. Perhaps the research environment and the route to funding has been more oriented at publications and other metrics than IP related and other commercialisations. So, I think the correct answer to that is perhaps we do need to pay more attention to that rather than be so focused on the academia. To offset that I think we are now more aware of that and if we have an idea in the lab we do go straight to legal representatives to see if its patentable and then we might seek venture capital to leverage those sorts of things but, gee, you need to have a pretty compelling story to build it from the ground up and I guess if you get it to the point where it's promising enough, then it might be something pharma would swoop in on.

Professor Ricky Johnstone: I think the problem in the country at the moment, with funding being squeezed or less available, the statistic is that the NHMRC (for the major project funding around) funded 11.9% of all applications. So that's more than 3,000 applications were made and 11.9% were funded. 160 hours per grant was spent and when you think about, that's wasted time and effort. So what happens when funding gets squeezed is that safe science tends to get funded. So there's no incentive for anyone on this panel to go out and put the effort in to try and come up with something really innovative. So, we need to be able to fund these things. There are now, surprisingly and encouragingly, some organisations that are putting their hand up to try and fill these funding gaps. The Cancer Council of Victoria put up these venture grant schemes which are specifically for 'blue sky' projects. "Have a crack! Do something really innovative. If it fails, it fails but we're going to fund you to have a go at it." So, we need more innovative funding streams like that. The problem with the country at the moment is that when funding gets tight, everyone shrinks down a little bit, things get safe and you squash innovation. And you block the ability to invent a new Dr.ug because you can't do it on the smell of an oily rag, you actually need some resources to do it. I can guarantee you that the figure of NHMRC will fund less than 11.9% this year and that's a major problem. If we're going to be the innovative country then let's put some money into it. Now you might want to lead into the

Future Fund Miles, it's a nice segue. Because that's been put up as the 'white knight' for research in this country. A $20 billion endowment and how that's going to flow down. We still don't know how we're going to use the money and I think $10million has flowed out so far. So where's the money? And let's start to think about ways to use it.

23. **MP: So my comment would be, that underlying all that is the researcher's security …. we're dealing with humans, aren't we? Look around the room, we're fortunate enough that we've got the most passionate people here and part of the reason that they can do their research is because they're in institutions that have the capacity. But, there's a lot of people who are screaming out to get funding so that they can allocate some time in their day to do the sort of stuff that they want to do. Fortunately the Victorian Cancer Agency are very supportive, there are a lot of fellowships that have come through that. Some of these guys in this room have had that, so I think there is that culture, certainly in Melbourne and Victoria, for that sort of recognition that money needs to be put aside so that people in their day can do the research. But one of the problems is getting young scientists in is the lack of long-term security and viability.**

Any questions from the audience?

Amanda Jones, Snowdome Director: You touched on the approach to research "if you fail, you fail". It's actually important sometimes to fail, to learn from those failings. There are surely equal learnings in failing?

Professor Ricky Johnstone: Yes, you learn from failings but it's not just in terms of that specific project. It's how you go about it and what mistakes you've made and how you wouldn't do it the next time. But you can only learn those things from experience. You've got to be encouraged to try to do the most innovative things, because if you're successful it could potentially change history so we have to be bolder and be encouraged to be bolder.

And I think, if you ask about the difference between us and the U.S. Miles, there's a different spirit over there about entrepreneurship and it flows through into the scientific world. Our colleagues at Memorial Sloan Kettering and Dana Farber, they are challenged to fail all the time. And, in fact, they're rewarded for that. And I think we've got to get to that sort of mind set.

MP: So, just to finish off, Piers can you tell us a story about your discovery recently of a new disease. Can you just explain how our 'new' understanding of genomics led to the discovery of this new condition?

Dr. Piers Blombery: Yes. There's a rare breast lymphoma that's associated with breast implants and no one really knows why it occurs. It looks like another sort of lymphoma that's very aggressive but in this case if you remove the implant, the lymphoma goes away so it's not like its normal counterpart.

So, we took some samples from two women with this breast implant associated lymphoma and we looked through the entire genome of these two patients and we found two interesting things. First of all, the drivers of this lymphoma are exactly the same as the drivers of the aggressive type that people need a lot of chemotherapy for to survive. But if you take the implant out, it goes away. The second is we found mutations, not in the cancer cells but in the patient's germline cells, ie. every cell in their body which actually keys up the immune system and what we think is happening is that the breast implants get a film of bacteria over them which doesn't cause an infection but just sort of sit there and basically 'tickle' up the immune system for years on end and if you've got the wrong sort of immune system with the wrong gene that you eventually go on to develop an immune cancer, such as lymphoma. So initially, we've found this in these two patients (and we've published this recently) but we've found at least another case where the patient's had the same germline predisposition to having this 'tickled' up system and developing cancer. So, I guess we've taken a disease where we had no idea why some women get and some don't and it's incredibly rare. The minority of people with breast implants get it and we didn't know why but now we've got at least some hypotheses to work out why some women get it and something to target and being able to advise them about their risk of getting it.

MP: So is your work potentially looking at the capacity to test people for predispositions and look at the genome to see whether they're predisposed to cancers?

Dr. Piers Blombery: That's right. So, specifically for these patients, two of them have a strong family history of breast cancer which is relevant for their daughters so the question of breast implants needs to be integrated into their decision making process. So there are implications for those patients but it's lead to international collaboration so we can see if it's a widespread phenomenon.

MP: I think what we've heard this morning is a lot about what causes cancer, a lot about what we have to understand, a lot of the hard work that needs to be done ahead, a lot of passion and I think also a lot of vision and I think what excites me most about today is we've got incredibly youthful minds and we're very proud to be involved with them and support them. It's been an exciting morning that will hopefully give you some insight into what makes these guys get up in the morning. Thank you to the panel and thank you for doing what you do every day.

To the audience … on behalf of Snowdome, thank you for coming today and for your broader support so these guys can do their work.

Please see next pages for BIO summaries for each member of today's panel.

BIOGRAPHIES

- Dr. Mary Ann Anderson, MBBS, FRACP, FRCPA

Mary Ann is a clinician scientist focusing on new treatments for leukaemia and lymphoma. She studies potential anti-cancer agents that target proteins which keep cancer cells alive. The long term goal is to develop better treatments for people with cancer, without the serious side effects of chemotherapy.

Her PhD research has focused on the BH3 mimetic agent, ABT-199, assessing it as a potential new treatment for people with certain leukaemias and lymphomas. She conducts laboratory studies to assess ABT-199's effects on leukaemia and lymphoma cells. As a haematologist Mary Ann is involved in clinical studies investigating ABT-199 as a potential new anti-cancer agent.

- Dr. Piers Blombery, BSc(Biomed), MBBS (Hons), FRCPA, FRACP

Dr. Piers Blombery is a clinical and laboratory haematologist and the medical lead of the molecular haematology laboratory in the Peter MacCallum Cancer Centre. After beginning his haematology training in Melbourne, he completed his training and worked as a consultant at University College London Hospital (UCLH) in the leukaemia/MDS service and the Specialised Integrated Haematological Malignancy Diagnostic Service. Along with a highly dedicated scientific team, he coordinates the provision of personalised therapy for patients with haematological malignancy at Peter MacCallum through comprehensive and tailored genomic assessment of blood cancer in the diagnostic laboratory. This work was pioneered in multiple myeloma and now extends to all types of haematological malignancy including chronic lymphocytic leukaemia, indolent lymphoma, aggressive lymphoma and the full spectrum of myeloid malignancies. Clinically he works in the aggressive lymphoma service and provides a consultative service in personalised molecular medicine.

- Dr. Michael Dickinson, MBBS (Hons), FRACP, FRCPA

Michael Dickinson is a Clinical Haematologist and Researcher who practices at Peter MacCallum Cancer Centre. He is Melbourne-trained and has also trained at the Royal Marsden Hospital in London. He has over 30 peer-reviewed publications and currently leads local and international clinical trials of new treatments for blood cancers. He is the Julie Borschmann Research Fellow at the University of Melbourne and is the Stream Lead for Aggressive Lymphoma at Peter Mac. Michael is driven to provide the best personal approach in the care of his patients.

- Professor Ricky Johnstone, PhD, FAAHMS

Professor Ricky Johnstone, Head of the Gene Regulation Laboratory at the Peter MacCallum Cancer Centre, received his PhD from the University of Melbourne in 1993 and after a postdoc at Harvard Medical School returned to Melbourne to establish the Gene Regulation Laboratory at the Peter MacCallum Cancer Centre in 2000. Professor Johnstone is the Associate Director of Laboratory Research at the Peter MacCallum Cancer Centre and plays a key role in defining the strategic direction of the research division. He has published more than 190 peer-reviewed papers, was awarded an NHMRC Senior Principal Research Fellowship in 2015 and in 2011 was promoted to Full Professor in the Department of Pathology at the University Of Melbourne. He is a cancer researcher who has utilized genetic mouse models of hemopoietic malignancies and solid tumors to understand the epigenetic changes that underpin tumor onset and progression and to develop new therapies that target epigenetic and transcriptional regulatory proteins. In 2008 Dr. Johnstone and Dr. Grant McArthur established the Cancer Therapeutics Program within the Peter MacCallum Cancer Centre

to bring together a critical mass of researchers with the aim to translate fundamental research findings into clinical outcomes that will benefit cancer patients.

- Professor Sharon Lewin, FRACP, PhD, FAAHMS

Professor Sharon Lewin is the inaugural Director of the Doherty Institute. She leads a large multi-disciplinary research team that focuses on understanding why HIV persists on treatment and developing clinical trials aimed at ultimately finding a cure for HIV infection and understanding how HIV interacts with other common co-infections, including hepatitis B virus (HBV). She is a consultant infectious diseases physician at the Alfred Hospital in Melbourne and an Australian National Health and Medical Research Council (NHMRC) Practitioner Fellow. She was recently appointed to the NHMRC Council and the Chair of the Health Translation Advisory Committee. Sharon was previously Head, Department of Infectious Diseases, the Alfred Hospital and Monash University (2003 – 2014) and Co-head, Centre for Biomedical Research, Burnet Institute (2010-2014). Sharon was the local co-chair of the XX International AIDS Conference (AIDS2014) held in Melbourne in July 2014, which was the largest health and development conference ever hosted in Australia. She is on the leadership team of the International AIDS Society's Strategy Towards an HIV Cure and is Chair of the Australian Government Ministerial Advisory Committee on Blood Borne Viruses and Sexually Transmitted Infections. Sharon was appointed as a Director of Snowdome in December 2014 As a clinical scientist, she is passionate about how investment and innovation in science can rapidly translate to new treatments and ultimately to saving lives. She believes that Snowdome bringing the latest scientific developments in cancer treatments directly to patients in Australia is a model we should use for many other diseases.

- Dr. Carrie van der Weyden, MBBS (Hons), FRACP, FRCPA

Dr. van der Weyden graduated from University of New South Wales with Honours in 2005, and completed her Haematology Specialist training in 2014, having worked in both city and rural hospitals in New South Wales during this period. She undertook a predominantly clinical fellowship at Peter MacCallum in 2015, and continued on in a research fellow position in 2016. She also commenced a D Med Sci at University of Melbourne in 2016. Carrie's research focus is predominantly in T cell lymphoma, with an interest in both genomic profiling and clinical trials in this field.

- Associate Professor Jake Shortt BMedSc MBChB FRACP FRCPA PhD

Associate Professor Jake Shortt is the Head of Haematology Research at the School of Clinical Sciences at Monash Health and clinical lead at Monash Haematology for leukaemia and myelodysplasia. He is principal investigator on a number of clinical trials, including multi-centre sponsored studies in leukaemia related disorders and investigator-initiated grant-funded trials in multiple myeloma.

Associate Professor Shortt is the recipient of an "Eva and Les Erdi" Snowdome Foundation / Victorian Cancer Agency (VCA) Fellowship for "New Targets in Haematological Malignancy" and is also in receipt of NHMRC, VCA and CCV project grant funding. He is an investigator on the Melbourne Genomics Health Alliance "Aggressive Lymphoma Flagship" and chairs the Laboratory Sciences Committee of the Australasian Leukaemia and Lymphoma Group (ALLG). His translational work in the School of Clinical Sciences at Monash Health is focused on strategies incorporating epigenetic drugs with immunotherapy in haematological cancers.