SNOWDOME FOUNDATION Donor Event

30 August 2017

Purpose of function: to present an interactive session of Snowdome funded researchers to highlight cutting-edge research and how philanthropic donations are making a difference.

Host: Professor Miles Prince, co-Founder & Director of Snowdome Foundation

Snowdome's mission

'accelerating new treatments to Australian blood cancer patients to help them live longer, better lives'

To achieve our mission, we support the Australian researchers who are working on delivering next-generation treatments. Prof Miles Prince (MP) led Snowdome researchers on an informative Q&A session.

MP: Michael, why is genomics so important?

I guess the simple answer is that some of these results determine treatment choice. So, in a patient who's never had treatment before, some of the simpler genetic tests that we do can help determine what kind of chemotherapy, and the intensity of chemotherapy, and what our approach is. It also can help refine exactly what the disease is that we're looking at. And so that means that over time when we look at how we've treated these patients, we can understand better what the outcomes of our treatments are as a group. But the most real example is when you find mutations that you can target with novel drugs. And we don't use novel drugs usually in the frontline setting, except for some of our more recent immunotherapy studies. But, in patients whose Lymphoma misbehaves, there's an opportunity to use novel drugs and the most pressing example that comes immediately to my mind is a trial that we're doing at the moment of EZH2 Inhibitor which is where we deliberately use a tablet to target a mutation that occurs in some forms of Lymphoma called an EZH2 mutation. And because we've been able to integrate this sort of genomic testing into our routine care, we're able to think one step ahead. So I've recently had an unfortunate patient whose Lymphoma's misbehaved, where I knew before the Lymphoma misbehaved that she had this mutation. So, when it did relapse, I knew that I had a broader range of treatment options than I might have had, had we not done the sequencing, and had Piers not been one step ahead, and provided me with that information as I needed it. So, it's really important, particularly for some patients who are more unlucky.

MP: Piers, how many genomics reports would you currently conduct each week?

We currently sign out about sixty or seventy of these reports a week. So, when we started doing this two years ago, we would do a run, which is about 20 cases, every fortnight. Now we do three runs a week. So, it's about sixty a week. Two hundred a month. And the majority of those contribute somehow to diagnosis therapy, or prognosis. And that's just Next-Generation Sequencing. So that's just the basic multi-gene mutation testing.

MP: Mark, how does genomics relate to personalised medicine?

The concept of personalised medicine is going to go through a very tough time in the next decade. Will we ever get to a point in time whereby a patient comes to see one of us, has their genome sequenced, and walks away with a cocktail of drugs? We might do. But what's important to recognise is that that cocktail will change the next time that person comes in. So your cancer is not static. And it will automatically adapt the moment it sees a challenge. Any challenge. Environmental, therapeutic, etc. So personalised medicine, to me is a concept that says that you're making an informed decision about the biology of the cancer that you could not have made without the advances in understanding that we have made.

MP: Mary Ann, can you treat cancer without chemotherapy?

I certainly see that the field is moving towards more targeted therapies, smarter therapies that try to specifically inhibit certain elements that are fundamental to the cancer, but not other cells. And I think that that's going to be increasingly used to get more effective therapies for our patients, and also to get therapies that are less toxic to our patients than the traditional ones.

MP: Wayne, what drives you as a researcher?

Well, making a difference ultimately. The reason I got into science is because I love it. I love learning, so that's what attracted me to University, and an undergraduate degree in pure sciences.

Sean?

First of all I'm so glad that Wayne said that the reason why he's doing this is because he wants to make a difference, and I think for everyone sitting up here, that's one of the reasons why we do research. Because you're committed. The wow factor is great when you just make a discovery, but as you get older, and certainly when you're working in biomedical research, you want to make a difference. And that's where we're focused. I have been very fortunate in my career, to have had some exceptional mentors and very, very open thinking supervisors that realise there is an incredibly important role in mentoring young intermediate researchers, and giving them the runway they need to come forward and do research. So that means that rather than just being the senior researcher, you work out how you build a portfolio to bring these people through. I think that's absolutely essential. There's no doubt that, as a scientist we need to be far more open-thinking about how we pursue funds these days. Whether it be with industry. Whether it be working through different efforts with state government, and federal government. And of course, philanthropy is absolutely vital. In many respects, it gives us the tip of the spear where we can take something that's aspirational that does not necessarily fit within the box, that maybe some of our federal funding bodies will look at, and can really allow us to make a difference quickly.

Miles, what drives your research?

What drives my research is probably the need to get better outcomes for other patients. So, it's about seeing a patient in front of me thinking I can do better. I know that some patients are cured with the treatments we have today, but a lot of patients are not. And my drive is to find better outcomes with better drugs, know more about the patient's disease. So, my main areas of research are about personalising the medicine, finding the personal aspects of that patient's cancer, and matching that with the best treatments. And the second is, embracing the power of the immune system, and working out how best to use the immune system to fight cancers.

MP: Mark what does philanthropic funding bring to research?

The funding climate for research at the moment is really difficult. Unfortunately, we live in an environment where what is funded is iterative work. You know, for you to get a government grant through the NMHRC system, or indeed, even through the ARC system, you need to establish that you have a track record. And there the best chance of success is previous success which young people actually find very difficult to do. Secondly, you also have to show feasibility, that you can actually do this. And for that, you need to have a relatively established environment, etc. And so by and large what we get is people who are doing research which answers an incremental question get funded to answer the next incremental question. And the difficulty there is that it's very hard to pursue truly innovative curiosity – ideas, that will change the natural history of diseases, not incrementally improve it, but completely change it. The philanthropic dollar is exceedingly important. It helps underpin what I call Blue Sky research. Because philanthropists, genuinely give. But you give

it with trust that you're giving it to the right individual who's going to ask a question that has not previously been answered, that will really make a fundamental difference.

MP: Mark, what may predispose you to cancer? OR Can genomics be used to predict cancer?

I guess the other way to interpret your question, potentially, is how can we prevent it? How can we stop it getting worse? It's an interesting question because it's an area that is so understudied: how do we prevent it? But by and large, that is because we don't understand what causes a majority of cancers. For smoking-related cancers, that's pretty easy. But if we take diseases such as the blood cancers that we've been talking about, we don't actually know what predisposes people to them. What are the environmental pressures that give rise to someone getting a cancer? Having said that, the advances in technology have enabled us to detect cancer at a much earlier rate. So there no longer has to be a football before it's diagnosed. And there are many areas by which we are trying to do this – one of this is genomics. And we may get to a time whereby we may be able to apply genomics as screening, especially in patients whom we recognise as having higher risk of getting cancers. What we do with that knowledge, and how we prevent it is a different question.

Miles, why are you so passionate about Snowdome?

Why am I passionate about Snowdome? I'm passionate about Snowdome because it is going to be a game-changer. Snowdome is there to accelerate new treatments, and it's doing that. I'm passionate because we've achieved so much, but I'm really passionate because it's got so much potential. I can see what a difference we're making. Snowdome is about making a difference, and I'd say right now we are making a difference, and that's what makes me excited.

Miles, what is your vision for Australian patients with blood cancer?

My vision is a simple one: which is a world without chemotherapy. A world without chemotherapy for patients with blood cancers is realistic. It's a realistic goal, and that's my vision.

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

Mary Ann is a clinician scientist focusing on new treatments for leukaemia and lymphoma. She studies potential anti-cancer agents that target proteins 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 Wayne Crismani PhD

Wayne joined the St Vincent's Institute Genome Stability laboratory in April 2016 after previously working at INRA (France) and then DuPont Pioneer, on the role of Fanconi anaemia proteins in DNA repair in model organisms. He is working on finding new modulators of DNA repair processes in humans, that have implications for cancer initiation and chemotherapy treatment.

He was recently awarded a Fellowship and Grant-in-aid by Maddie Riewoldt's Vision (Maddie's Vision) to pursue research into Bone Marrow Failure Syndromes (BMFS), to can gain a better understanding of what triggers bone marrow failure, and use that knowledge to further research into how to prevent it from occurring.

- Professor Mark Dawson MBBS(Hons) BMedSci FRACP FRCPA PhD(Cantab.)

Professor Dawson is a clinician-scientist at the Peter MacCallum Cancer Centre. He is the program head of the Translational Haematology Program, Group leader of the Cancer Epigenetics Laboratory and Consultant Haematologist in the Department of Haematology. His research interest is studying epigenetic regulation in normal and malignant haematopoiesis. He is a fellow of the Royal Australasian College of Physicians and Royal College of Pathologists of Australasia. After completing his clinical training in Melbourne, Australia he was awarded the prestigious General Sir John Monash Fellowship and Cambridge Commonwealth Trust Fellowship, which he used to complete his PhD at the University of Cambridge. During his PhD, he described one of the first examples of how a signaling kinase can directly influence transcription by acting as a histone-modifying enzyme. Following his PhD, he was the top ranked applicant for a career development fellowship in the UK and was awarded the inaugural Wellcome Trust Beit Prize Fellowship to pursue his research into epigenetic regulation of leukaemia stem cells. This research identified a new therapeutic strategy for acute myeloid leukaemia by targeting the BET bromodomain proteins that function as epigenetic readers. This work helped set the platform for clinical trials with this first in class epigenetic therapy. His research has been published in world leading journals including Nature, Cell, Science and New England Journal of Medicine. He is currently a Professor in the Sir Peter MacCallum Department of Oncology and Centre of Cancer Research at the University of Melbourne. He is also the Senior Research Fellow for the Leukaemia Foundation of Australia and a Howard Hughes Medical Institute International Research Scholar.

- 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 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. He has over 30 peer-reviewed publications and currently leads local and international clinical trials of exciting new treatments for blood cancers that harness epigenetics and immunology to have their effect.

- Dr Lucy Fox BCom/BSci, MBBS, FRACP, FRCPA

Lucy is currently a Clinical Haematology Fellow at Epworth Healthcare and also a Molecular Haematology Fellow at the Victorian Comprehensive Cancer Centre. Her previous haematology training was completed at the Australian Red Cross Blood Service, Austin Hospital (Melbourne), St Vincent's Hospital (Melbourne) and the Royal Hobart Hospital.

- Professor Sean Grimmond BSc PhD FFS RCPA

Professor Grimmond obtained his PhD in pathology from the University of Queensland. He is a founding scientific fellow in The Royal College of Pathologists of Australasia. Previous appointments include the chair of medical genomics at the University of Glasgow, co-director of the Scottish Genomes Partnership, a professor of genetics at the University of Queensland, and founding director of the Queensland Centre for Medical Genomics.

Over the past 8 years, Sean has pioneered whole-genome and transciptome analysis of cancer patients, led Australia's International Cancer Genome Consortium efforts into pancreatic, neuroendocrine and ovarian cancer, and contributed cohort-based mutational landscape studies in melanoma and oesophageal cancer. These studies have been used to resolve the mutagenic processes, driver mutations, molecular taxonomies, and potential vulnerabilities open to therapeutic

exploitation in these cancer types. His current research is firmly focused on real-time omic analysis of recalcitrant cancers, testing the value of personalised therapies, and further cancer genome discovery.

- Associate Professor David Westerman MBBS, FRACP, FRCPA, FFSc

Associate Professor David Westerman is an Australian-based health professional. David is trained as a Physician & Haematologist (Blood Disorders Specialist), Haematopathologist (pathologist) and has been the Head of Haematopathology at the Peter MacCallum Cancer Institute for 20 years. He is Chair of the Hospital Transfusion Committee, Deputy Director Department of Pathology Peter Mac, while he holds honorary appointments at the Department of Pathology, University of Melbourne and Sir Peter MacCallum Department of Oncology.

- Dr Paul Yeh BMedSc MBBS FRACP FRCPA

Dr Yeh is currently undertaking his PhD and was awarded the George & Yolanda Klempfner Fellowship facilitated through the Snowdome Foundation in 2015. Paul is working under the guidance of Professor Mark Dawson. He is also a co-investigator in many clinical trials involving novel treatments for haematological cancers.

Dr Yeh completed his medical degree from the University of Melbourne in 2005 where he also awarded his first research degree (Bachelor of Medical Science). He undertook physician training at the Austin Hospital and was the Elizabeth Austin Registrar for 2011. He completed his haematology training in 2015 at Peter McCallum Cancer Centre, Austin Hospital and Melbourne Pathology. He is a fellow of both the Royal Australasian College of Physicians and Royal College of Pathologists of Australasia and is a member of the Haematology Society of Australia & New Zealand (HSANZ).

- Professor Miles Prince AM MBBS (Hons) MD FRACP FRCPA AFRCMA AFRACD FAHMS

Miles is a Professor of Medicine at both Melbourne and Monash Universities and Professor/Director of Molecular Oncology and Cancer Immunology at Epworth Healthcare and Director of the Centre for Blood Cell Therapies at the Peter MacCallum Cancer Centre, Melbourne. He trained in Melbourne, Sydney and Toronto. He holds Fellowships in the Royal Australasian College of Physicians, Royal College of Pathologists of Australasia, Royal Australian College of Medical Administrators, Australasian College of Dermatologists and is a Fellow of the Academy of Health and Medical Sciences. He has a very active research program involving clinical research and laboratory research – the latter involving stem cell research, cell engineering [www.celltherapies.com.au] and cancer immunology [www.petermac.org/Research/CancerImmunologyProgram]. He has been involved in dozens of clinical trials of new therapies for blood cancers such as leukaemia, lymphoma and myeloma and holds prestigious grants including being a chief investigator for a $12.5M Program Grant from the NH&MRC in cancer immunology, and large translational research grants from the Leukemia Lymphoma Society of America, the European Union Collaborative Grants and US National Institute of Health. He is the leader of an epigenetics consortium funded by the Victorian Cancer Agency and is currently the Chairman of the medical scientific advisory group to the Myeloma Foundation of Australia and on the board of the MFA and Chairman of the Australian T cell Lymphoma Network and on the Board of the International Society of Cutaneous Lymphoma. He has published over 400 peer-reviewed manuscripts and is a reviewer for numerous scientific journals and medical advisor to a variety of government and pharmaceutical bodies. In 2015 he was awarded a Member of the Order of Australia for services to haematology research, patient care and philanthropy leadership.

Snowdome's achievements since October 2010

- **254** Australian blood cancer patients gained access to new treatments through **15** clinical trials with Snowdome support
- **220** patient samples to support biomarker studies
- **160** Australian blood cancer patients to receive personalised treatment
- Raised over **$20 million** and operates at **less than 15% expenses to revenue**

Snowdome Granting Principles

- Accelerate new therapies to Australian blood cancer patients in the foreseeable future
- Support Australian researchers in Australia
- Involve new therapies that are part of the 'pillars' of blood cancer therapies
- Establish quantifiable outcomes and reasonable preset milestones
- Deliver research (clinical or laboratory) that identifies patients that are likely to benefit from new therapies (that exist now/foreseeable future)

Snowdome's Granting Achievements

To date, over 80% of funds raised have already been committed to blood cancer research:

Genomics Research:

- $5.5M for Christine & Bruce Wilson Centre for Lymphoma Genomics at Peter MacCallum Cancer Centre: **A/Prof David Westerman**
- $3M to launch Myeloma@VCCC/UoM: **Dr Michael Dickinson**
- $300K for Vision Super-Snowdome Foundation Fellow: **Dr Piers Blombery**

Biomarker Research:

- $260K for Gandel Philanthropy-Snowdome Innovation Fellow: **Dr Mary Ann Anderson**

Epigenetics Research:

- $800K for Erdi-Snowdome Fellow with Victoria Cancer Agency (VCA): **A/Prof Jake Shortt**
- $250K for Klempfner Fellow: **Dr Paul Yeh**
- $4.8M+ into numerous trials support at Peter Mac, The Alfred, Royal Melbourne, WEHI, and Monash involved in the Victorian Epigenetics Group (co-funded with VCA)

Bone Marrow Failure Research:

- $1M Maddie Riewoldt's Vision: 2 Fellowships awarded, 3 Grant-in-aids and the first National Aplastic Anaemia Registry:
  - **Dr Wayne Crismani** – Maddie's Vision Fellowship 2016 & GIA recipient ($286K)
  - **Dr Piers Blombery** – $200K Grant-in-aid
- $300K for Snowdome-Maddie's Vision Fellow for bone marrow transplant research: **Dr Paul Yeh**

Snowdome's Advantage:

- Work with major donors interested in funding blood cancer research.
- Match 'donor wishes' to cutting-edge research opportunities within Snowdome's funding principles.
- Most major donations do not have any Snowdome administration expense.
- Effective at seeking government matched-funding opportunities.