Sydney Catalyst
Postgraduate and
Early Career Researcher
Symposium 2018

ABSTRACT BOOKLET AND PROGRAM

Wednesday 2nd May, 2018
On behalf of the Organising Committee, it is my pleasure to welcome you to the 2018 Sydney Catalyst Postgraduate and early-career researcher (PG&ECR) symposium. I have been a proud member of Sydney Catalyst for over 3 years. I can recall fondly returning to Sydney from my overseas postdoc eager and excited to present my ‘pet project’ in the PG&ECR symposium. A rewarding experience I am pleased to have built on.

Sydney Catalyst has more than 500 members across approximately 30 member groups in NSW, with a key focus on facilitating member opportunities for professional development, communication, and collaboration across the consortium. The annual PG&ECR Symposium is a cornerstone of the Sydney Catalyst event calendar, as it provides a unique opportunity for postgraduate students and early-career researchers from across the translational spectrum to come together and learn from each other. As you will see there is great diversity in the presentations ranging from basic sciences, clinical trials and studies, psychosocial and implementation research.

And this year we are delighted to welcome an additional format to help facilitate networking across our members - the “Virtual Symposium”. I hope you have been enjoying the posters shared online already, and find time throughout the lunch and networking drinks to meet with our presenters and strike up a conversation about their work (look for the yellow dots on name tags to identify our virtual poster participants).

We are also excited to welcome Professor David Thomas as our opening keynote speaker, whom will be sharing his experience in career development in translational cancer research. We’ll learn about David’s experience working in genomic cancer research and gain insights into skills he thinks are important for emerging researchers to be successful. Today’s program also includes an thought provoking panel discussion continuing the theme of essential skills and insights for developing a successful career in translational cancer research. We are incredibly grateful for the time our panellists are taking to be with us today; thank you Dr Prunella Blinman, Professor Phyllis Butow, Associate Professor Chris Milross and facilitator Professor Lisa Horvath.

I have thoroughly enjoyed being involved in the planning for this Symposium and would like to thank the other members of the organising committee; Dr David Croucher, Marissa Williams, Amelia Smit and Eve Simons, as well as the Sydney Catalyst Central Office team for all their hard work behind the scenes to make this event happen. I would also like to give particular thanks to Danielle Miller for her wonderful support of the organising committee. We wish her all the very best for her future endeavors. Finally, I would also like to take this opportunity to thank Professor John Simes for this role as Director of Sydney Catalyst and welcome Professor Michael Boyer. Sydney Catalyst looks forward to continue building a bright future under new leadership.

We hope this year’s Symposium will give you an appreciation of the breadth of excellent research being conducted by your peers and colleagues and that you take with you inspiration, cutting-edge knowledge and new contacts.

Dr Helen McGuire, Chair, PG&ECR Symposium Working Group

WORKING GROUP

- Dr Helen McGuire (Chair), Research Officer, Charles Perkins Centre, The University of Sydney
- Dr David Croucher, Group Leader - Network Biology, The Kinghorn Cancer Centre, Garvan Institute of Medical Research
- Marissa Williams, PhD Student, Asbestos Diseases Research Institute
- Amelia Smit, PhD Candidate and Research Study Coordinator, Cancer Epidemiology and Prevention Research, The University of Sydney
- Eve Simons, Sydney Catalyst Education Project Coordinator
KEYNOTE SPEAKER

Professor David Thomas
Director, Kinghorn Cancer Centre; Head, Cancer Division at The Garvan Institute of Medical Research

Keynote title: The translational cancer research spectrum – From discovery to implementation
David is Director of The Kinghorn Cancer Centre and Head of the Cancer Division, Garvan Institute of Medical Research. David undertook medical training at the University of Melbourne, completed post-graduate training as a Fellow of the Royal Australasian College of Physicians in Medical Oncology and was awarded a PhD (University of Melbourne) in 1997. David undertook post-doctoral research at Harvard Medical School (1998-2000), before moving back to Melbourne to set up his own laboratory, initially at St Vincent's Hospital (2001-3), then at Peter MacCallum Cancer Centre (2002-2014). David was the founding Chair of the Australasian Sarcoma Study Group (2007-11), and is currently a board member and Deputy Chair. His research interests focus on somatic and germline cancer genomics, with a focus on sarcomas and cancer in young adults.

PANEL DISCUSSION

Facilitated by Professor Lisa Horvath
Panel topic: Developing a successful career in translational cancer research
- Dr Prunella Blinman, Medical Oncologist, Concord Cancer Centre & Clinical Senior Lecturer, Sydney Medical School
- Professor Phyllis Butow, Chair Sydney Catalyst Scientific Advisory Council
- Associate Professor Chris Milross, Director of Radiation Oncology and Medical Services, Chris O’Brien Lifehouse

PARTICIPANT FEEDBACK SURVEY

What did you think of the Sydney Catalyst Postgraduate and Early Career Researchers Symposium?
Did you enjoy the day but have some suggestions for how we can improve for next time?
Can’t wait to share your feedback with us?

Log into our online program evaluation now and tell us what you thought!

https://www.surveymonkey.com/r/2018pgecrs
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<td>9.15-9.45am</td>
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| 9.45-9.50am  | Introduction - Dr Helen McGuire - Chair - Postgraduate and Early Career Researcher (PG & ECR) Symposium Working Group  
Ramaciotti Facility of Human Systems Biology, The University of Sydney  
Welcome  
Professor Michael Boyer, Director of Sydney Catalyst |
| 9.50-10.20am | Keynote  
Professor David Thomas  
Director, Kinghorn Cancer Centre; Garvan Institute of Medical Research  
The translational cancer research spectrum – From discovery to implementation |
| 10.20-10.30pm| Question and answer time with Professor David Thomas                |
|              | Session 1: Chaired by Amelia Smit - PG & ECR Symposium Working Group  
PhD candidate, Cancer Epidemiology and Prevention Research team and  
Sydney Health Ethics, School of Public Health, The University of Sydney |
| 10.30-10.45am| Abstract Presentations (10 min presentations + question time)         |
| 10.30-10.45am| Priyanka Tharkar, PhD Candidate, The University of Sydney  
Fabrication, optimization and characterization of ultrasound-responsive solid lipid nanoparticles for oxygen delivery in lung cancer treatment |
| 10.45-11.00am| Julius W. Kim, Post-Doctoral Fellow, Dendritic Cell Research, ANZAC Research Institute  
Blood Dendritic Cell Based Vaccine Therapy and a Potential Combinatory Therapy with Checkpoint Inhibitor(s) against Brain Tumours |
| 11.00-11.15am| Alison Young, PhD/M Psych (Clinical) Candidate, The University of Sydney  
What is there to know? Knowledge and information preferences of young adults about BRCA1 or BRCA2 |
| 11.15-11.30am| Dr Beatriz Perez San Juan, Research Officer, Garvan Institute of Medical Research  
Inflammatory Response to Primary Breast Cancer Prevents Metastasis-Initiating cell Colonization |
| 11.30-11.45am| Morning Tea                                                          |
|              | Session 2: Chaired by Dr David Croucher - PG & ECR Symposium Working Group  
Group Leader - Network Biology, Garvan Institute of Medical Research |
| 11.45-12.00pm| Abstract Presentations (10 min presentations + question time)         |
| 11.45-12.00pm| Kriscia Tapia, BREAST Project Manager, The University of Sydney  
BREAST: Transforming the detection of breast cancer |
| 12.00-12.15pm| Dr Camelia Quek, Postdoctoral Scientist, Melanoma Institute Australia  
Anti-PD-1 monotherapy versus combined anti-PD-1 and anti-CTLA-4 immunotherapy in metastatic melanoma: who will benefit? |
| 12.15-12.30pm| Dr Megan Best, Cancer Institute Post-doctoral Research Fellow, The University of Sydney  
Young cancer patient perspectives on undertaking whole genome sequencing:  
A qualitative study |
| 12.30-12.45pm| Dr Ben Kong, PhD Candidate, Anzac Research Institute  
Glioblastoma multiforme |
| 12.45-1.00pm | Dr Erin Moth, Clinical Research Fellow, Concord Repatriation General Hospital  
Predicting chemotherapy toxicity in older adults: comparing the value of the CARG Toxicity Score with oncologists’ estimates of toxicity |
<p>| 1.00-1.45pm  | Networking Lunch and Human Bingo                                      |</p>
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| 1.45-2.00pm  | Abstract Presentations (10 min presentations + question time)                                  | Cindy Li, PhD Student, Dendritic, Cell Biology and Therapeutics Group, ANZAC Research Institute  
CD83 is a new potential biomarker and therapeutic target for Hodgkin Lymphoma |
| 2.00-2.15pm  |                                                                                                 | Dr Yun Trieu, PhD Student, The University of Sydney (presenting on behalf of Ziba Gandomkar)  
The abnormal gist in the prior mammograms even without visible cancer sign |
| 2.15-2.30pm  |                                                                                                 | Jarem Edwards, PhD Candidate, Melanoma Institute Australia                               
The Landscape of immune checkpoint receptors in untreated human melanoma |
| 2.30-2.45pm  |                                                                                                 | Dr Jolyn Hersch, NHMRC Early Career Fellow, School of Public Health, The University of Sydney  
Clinicians’ perspectives on Ductal Carcinoma In Situ (DCIS) among older women: a qualitative study |
| 2.45-2.50pm  | Nominations and Voting for the People’s Choice Award                                           |                                                                                           |
| 2.50-3.45pm  | Panel Discussion + Q&A (40 mins discussion + 15 mins Q&A)                                      | Facilitated by Professor Lisa Horvath                                                      
Developing a successful career in translational cancer research                      
- Dr Prunella Blinman, Medical Oncologist, Concord Cancer Centre & Clinical Senior Lecturer, Sydney Medical School  
- Professor Phyllis Butow, Chair Sydney Catalyst Scientific Advisory Council  
- Associate Professor Chris Milross, Director of Radiation Oncology and Medical Services, Chris O’Brien Lifehouse |
| 3.45-3.50pm  | Presentation of Awards & Introduction of Virtual Posters                                       |                                                                                           |
| 3.50-4.45pm  | Networking Drinks                                                                               | ‘Live’ Virtual Poster Presentations                                                        |

**NETWORKING**  
Key to coloured dots on name tags for networking purposes

- Blue: Sydney Catalyst Governing Council, Scientific Advisory Committee, T1-T2 Working group and T2-T3 Working Groups
  Postgraduate and Early Career Researcher Symposium Working group
- Red: Speakers and panellists
- Yellow: Submitted a Virtual Poster
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**ABSTRACT**

Lung cancer kills more people than colon, breast, and prostate cancer combined. Tumor hypoxia is a pathophysiological characteristic of all solid tumors, and hyperoxygenation can promote tumor regression. Therefore, by delivering oxygen in a targeted manner it is possible to inhibit tumor growth. Our aim was to develop inhalable ultrasound-responsive solid lipid nanoparticles (SLNs) for oxygen delivery for lung cancer therapy. Perfluorocarbon (PFC) which is an active oxygen carrier was encapsulated into lipid based nanoparticles and its local release activated using focused ultrasound. Along with tumor targeting, ultrasound causes highly beneficial perturbation of cell membrane and enhance permission of nanoparticles to cell deeper penetration within ECM. Ultrasound responsive nanoparticles were fabricated and optimized and in vitro cytotoxicity of the formulations was determined using A549 and BEAS-2B cell lines by the CCK-8 and LDH assays.

Our studies demonstrated that ‘focused wave’ induced an increase in the nanoparticle diameter and fragmentation, which suggested that particles were sensitive to the ultrasound and are likely to release the PFC payload locally when exposed to ultrasound. The next steps involve the study of intra- and extra-cellular disruption of nanoparticles by ultrasound, followed by oxygen release study on normal and lung cancer cell lines.

**BIOGRAPHY**

Priyanka Tharkar is currently a PhD candidate at the Faculty of Pharmacy, University of Sydney. She has been awarded the W H & Elizabeth M Dean Pharmaceutical Fund PhD Scholarship by the Faculty of Pharmacy. She has gained research experience of working on advanced nanoformulations to target cancer cells at University of Auckland, NZ. She had also worked as full time Faculty Lecturer at Amravati University, India.

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**ABSTRACT**

**Background:** Cancer vaccines represent a novel and promising approach for aggressive neoplasms such as brain tumour where other treatment modalities have not been effective. In this regard, cancer vaccines have been developed which exploit the key central immunoregulatory dendritic cell (DC) to maximize vaccine efficacy. Such “DC vaccine” strategies are currently being evaluated clinically and form the basis of a few commercial initiatives. However, current monocyte derived DCs (Mo-DCs) based vaccines have shown limited efficacy, possibly due to insufficient antigen presentation capability as well as inability to migrate toward lymph nodes. In this regard, we have developed a novel antibody against the CMRF-56 antigen which preferentially select for distinct blood derived dendritic cell (BDC) subsets including myeloid CD1c+ and the highly efficient cross-presenting CD141+ BDC subsets.

**Question:** We investigated whether BDCs possess more efficient natural capability to induce immunity against cancerous cells especially brain tumour which may be enhanced with the addition of immune checkpoint inhibitor(s)

**Results:** Unlike commonly used monocyte-derived DCs (Mo-DCs) vaccines, requiring artificial induction of differentiation/activation to load tumour specific antigens, CMRF-56 antibody-based selected BDCs showed a highly activated/matured status upon selection. BDCs also showed the better migratory capability and respond to the lymph nodes-migratory signal (CCL7/CCL21).

Most importantly, antigen processing and presentation capabilities were superior to those of Mo-DCs, implying a highly efficient immunotherapeutic efficacy against GBM. In addition, we will discuss a potential boosting combinatory immunotherapeutic approach against GBM; BDC based vaccine in combination with checkpoint inhibitor(s)

**Conclusions:** We showed a therapeutic potential of a novel immune-combinatory personalised medicine against Brain tumour.

**BIOGRAPHY**

Julius received Ph.D. at Saint Louis University, U.S.A., researching on neuronal development and its related cell signalling. Over the past 5 years of Post-Doctoral period, he has been researching on anti-tumour immunotherapy; specifically, for the treatment of glioblastoma multiforme (GBM). In dendritic cell translational research, he has generated a novel dendritic cell targeted vector and patented for cancer vaccine approach in the USA. In GBM translational research, he has researched various therapeutic approaches. One of the projects that he participated in has been approved for a Phase I clinical trial (NCT03072134) in the USA, directly contributing for the treatment to patients with GBM.
Alison Young  
The University of Sydney

ABSTRACT
A striking feature of hereditary breast cancer is the younger age of onset, occurring frequently in the 30s and 40s and even in the 20s. Despite growing up in an era replete with breast cancer awareness, the hereditary cancer information and resource preferences of young adults aged 18-40 with a known BRCA1 or BRCA2 (BRCA1/2) gene mutation in their family is largely unknown. The current findings are drawn from two studies: young adults and their families with a known BRCA1/2 gene mutation (N=21 families) and health professionals (e.g., geneticists, genetic counsellors) working with families attending familial cancer clinics from five states of Australia (N=74). Discrepancies between health professionals’ views and that of young adults were noted including young adult’s desire to have screening/surgery earlier than recommended, the rationale for testing and emotional support. Health professionals perceived information about preventative measures and concern for the cancer risk of the next generation to be of paramount importance. Young adults reported a need for additional information about: key facts, cancer risk estimations and side effects of surgery. Recommendations for health services and the use of novel tools for delivery of information to young adults will be discussed.

BIOGRAPHY
Alison Luk Young is a psychologist and current Masters of Clinical Psychology/PhD candidate at the University of Sydney. Her clinical and research work has focused on supporting patients and their families in both adult and paediatric oncology. Alison’s research focuses on family communication, information needs, and genetic-related health professional’s experiences working with families with a BRCA1 or BRCA2 gene mutation. Alison has over four years of experience working in psycho-oncology research with both the Behavioural Sciences Unit at Sydney Children’s Hospital and currently with the Centre for Medical Psychology and Evidence-based Decision-making (CeMPED).

Dr Beatriz Perez San Juan  
Garvan Institute of Medical Research

ABSTRACT
Lack of insight into mechanisms governing breast cancer metastasis has precluded development of curative therapies. Metastasis-initiating cancer cells (MICs) are uniquely equipped to establish metastases, causing recurrence and therapeutic resistance. Using various metastasis models, we discovered that certain primary tumors elicit a systemic inflammatory response involving IL-1β-expressing innate immune cells that infiltrate the distant MIC microenvironment. At the metastatic site, IL-1β maintains the MIC mesenchymal-like phenotype but prevents MICs from generating highly proliferative E-cadherin-positive progeny. Thus, when the inherent plasticity of MICs is impeded, overt metastases cannot be established. Ablation of the pro-inflammatory response or IL-1R inhibition relieves the differentiation block and results in metastatic colonization. Among breast cancer patients, high primary tumor IL-1β expression associated with better overall survival and distant metastasis-free survival. Our data reveal complex interactions that occur between primary tumors and disseminated MICs that could be exploited to improve survival of patients at risk for metastasis.

One Sentence Summary: Metastatic colonization can be inhibited by preventing cellular plasticity of metastasis-initiating cells via an IL1-mediated innate immune response driven by the primary tumor.

BIOGRAPHY
I completed my PhD in Molecular Biology in 2013 and was awarded Cum Laudem and European mention. While undertaking my PhD, I worked as a researcher at the Severo Ochoa Molecular Biology Centre in Madrid, Spain, focusing on the identification and functional characterization of novel regulators of cell proliferation and differentiation, assessing their implication in tumour progression. In 2014, I moved to Australia and joined the Garvan Institute of Medical Research, where I worked for a brief period of time modeling pancreas regeneration in vivo. After this experience, I was recruited by Dr. Christine Chaffer to join the Cancer Cell Plasticity Laboratory (early 2016). Since then, I have worked uncovering the molecular basis underlying cancer cell plasticity and establishing its role in regulating metastatic and recurrence potential in breast cancer. This work is opening exciting avenues with the potential to develop novel therapeutic strategies.
**BIOGRAPHY**

Kriscia Tapia is the project manager of the BreastScreen Reader Assessment Strategy (BREAST). Kriscia is also a member of the Medical Image Optimisation and Perception Research Group (MIOPeG) at the University of Sydney as a PhD candidate with her study in Northern Territory Indigenous women’s mammographic density, breast cancer, and breast screening. Kriscia’s research interests include Indigenous health, markers of good and performance in radiology, lesion characteristics that impact detection, perception science in cancer detection, mammographic density, and new technologies in medical imaging.

**BIOGRAPHY**

Dr Camelia Quek is a medical researcher at Melanoma Institute Australia, The University of Sydney. Her early research in non-coding RNAs has bridged wet-lab based molecular biology and biochemistry with computational biology, making notable contributions to the new class of diagnostic biomarker in exosomes. She implements a multi-disciplinary approach of computational and molecular biology to unlock the underlying molecular mechanisms in complex diseases including neurological disorders and skin cancer. Her current research involved Phase I, II and III clinical trials in advanced metastatic melanoma, particularly focus on identifying molecular biomarker that correlates with response and resistance to cancer therapy. She designs and implements a scientific channel for high-throughput biomarker discovery using next-generation sequencing and bioinformatics for selecting patients who will obtain maximal benefit from treatment without experiencing drug toxicities and resistances to improve patient outcomes.
ABSTRACT

Background: Whole genome sequencing (WGS) is moving into clinical practice, with the goals of identifying gene variants that increase individuals’ risk of disease and guiding prevention strategies. However, little is yet known about the ethical, psychosocial and behavioural implications of WGS. The Genetic Cancer Risk in the Young Study is recruiting 1,000 young cancer patients and blood relatives to undertake WGS to investigate heritable genetic disease drivers. A young age at diagnosis increases the likelihood of inherited predisposition. The current psychosocial sub-study (PiGeOn) aims to explore participants’ motivations, understanding, experiences and views about WGS longitudinally. Baseline qualitative results are reported here.

Methods: Transcribed, semi-structured interviews of purposively selected PiGeOn participants (to ensure varied cancer types and demographics) were analysed using Framework analysis.

Findings: Data analysis of 18 patients (aged 32-78 years) interviewed to date identified five inter-related major themes: Motivation, Emotional readiness and response, Balancing individual versus relational aspects of autonomy, Balancing benefit versus harm, and ‘The black box’. Participants’ motivations include: seeking empowerment, opportunity, a sense of responsibility to family, solidarity with similarly-affected people, and curiosity. Participants viewed genomic information as: reducing uncertainty, offering protection, not to be feared, and important to act upon. All participants desired meaningful information that could inform action, and balanced this against personal and community costs. Participants often lacked full understanding and desired lay-appropriate explanations; but they, but felt embarrassed to request these. Most trusted the science of WGS and the research process. All recognised their results could have implications for other family members, but family culture influenced the degree of consultation before individuals consented.

Discussion: Young cancer survivors see WGS as an opportunity for the individual, family and wider community to reduce future risk. Participants had high hopes of actionable results. A cancer diagnosis may motivate patients and family members to be more active in managing their risk, but may need interventions to promote better understanding and communication within the family about WGS results. Most participants considered WGS to be beneficial and found the experience of testing to be positive. Support may be needed with family communication about testing and results.

BIOGRAPHY

Dr Megan Best is a Cancer Institute NSW Post-doctoral Research Fellow who works with the Psycho-Oncology Research Group (PoCoG) at the University of Sydney. She is a Co-investigator and Project Manager for two NHMRC-funded studies associated with the NSW Genomic Cancer Medicine Program, based at the Garvan Institute for Medical Research. These studies examine the psychosocial, behavioural and ethical impact of genomic screening for cancer.

ABSTRACT

Glioblastoma multiforme (GBM) is the most common primary brain tumour in Australia. It disproportionately affects younger adults with devastating neurological sequelae. Current treatments include surgery, chemotherapy and radiotherapy, however the prognosis for GBM remains poor. Dendritic cell (DC) vaccination is a promising strategy for cancer immunotherapy due to the ability of DC to induce antigen-specific responses. GBM is associated with systemic T cell dysfunction, however the role of other important immune system components, particularly DC is less well characterised. Therefore it is crucial to understand the function of immune cells in GBM patients to translate DC based therapies into the clinic. Blood dendritic cells (BDC), including the readily isolated CD1c+ (BDCA-1) subset, have shown superior antigen presenting capability compared to the more commonly used monocyte derived DC (MoDC).

Combination therapy with DC vaccination and immune checkpoint inhibition is a potential strategy for immunotherapy which takes advantage of DC driven control of antigen-specific responses as well as the ability of immune checkpoint inhibitors to remove tumour-associated immune suppression. To advance this strategy to clinical application, it is necessary to confirm the presence of functional DC in GBM, the expression of relevant immune checkpoint molecules in the immune system and the effect of combining these therapies in vitro. Here we describe a comparison of DC from healthy donors and GBM patients, focussing on immune checkpoint molecule expression, and the effects of immune checkpoint blockade with anti-PD-1 and anti-CTLA-4 monoclonal antibodies in DC-driven proliferative responses.

BIOGRAPHY

Ben Kong is a medical oncologist completing his PhD in cancer immunotherapy with the Dendritic Cell Research Group at the ANZAC Research Institute. He has a track record of clinical research in immunotherapy through working as a sub-
investigator on clinical trials of immune checkpoint inhibitors in solid tumours at Westmead Hospital and Melanoma Institute Australia. He is interested in the translation of novel therapies into clinical practice to improve response rates to current treatments. His PhD project is focussed on translation of DC therapies in combination with immune checkpoint inhibitors using glioblastoma multiforme (GBM) as a model system.

Dr Erin Moth
Concord Repatriation General Hospital

Predicting chemotherapy toxicity in older adults: comparing the value of the CARG Toxicity Score with oncologists’ estimates of toxicity

ABSTRACT

Purpose: The Cancer and Ageing Research Group’s (CARG) Toxicity Score was designed to predict grade ≥3 chemotherapy-related toxicity in adults ≥65yrs commencing chemotherapy for any stage or type of solid cancer. We aimed to evaluate the CARG Score in an Australian setting and compare it to oncologists’ estimates for predicting severe chemotherapy toxicity in older adults.

Methods: Patients aged ≥65yrs starting chemotherapy for a solid organ cancer (any type/stage) had their CARG Score (range 0-23) calculated. Their treating oncologist, blinded to these results, independently estimated the patient’s risk of severe chemotherapy toxicity (0-100%). Toxicities were captured prospectively. The predictive value of the CARG Score, oncologists’ estimates, and a combined measure was estimated using logistic regression and in terms of Area Under the Receiver Operating Characteristic curve (AU-ROC).

Result: 126 patients from 10 oncologists at 2 sites participated. The median age was 72yrs (range 65-84). The median CARG Score was 7 (range 0-17), and the median oncologist estimate of risk was 30% (range 3-80%), and these measures were not correlated (r=-0.01). 64 patients (52%) experienced grade ≥3 toxicity. Rates of severe toxicity in low-, intermediate-, and high-risk groups by CARG Score were 58%, 47%, and 58% respectively, and 63%, 44%, and 67% by oncologist estimate. Severe chemotherapy toxicity was not predicted well by the CARG Score (OR 1.04, 95%CI 0.92-1.18, p-value 0.54, AU-ROC 0.52), oncologists’ estimates (OR 1.00, 95%CI 0.98-1.02, p-value 0.82, AU-ROC 0.52), or a model combining the two (AUC-ROC 0.52).

Conclusion: The CARG Score, oncologists’ estimates, or a combination of the two, were not good predictors of severe chemotherapy-related toxicity in our local population of older adults. Methods to improve risk prediction are needed.

BIOGRAPHY
Erin Moth is a Medical Oncologist with an interest in improving treatment decision-making and supportive care for older adults with cancer, which is the focus of her current PhD studies. She is currently working at Concord Repatriation General Hospital, completing her PhD studies through Concord Cancer Centre.

Cindy Li
ANZAC Research Institute

CD83 is a new potential biomarker and therapeutic target for Hodgkin Lymphoma

ABSTRACT

Background: Hodgkin lymphoma (HL) is a B cell neoplasm that is defined by the presence of Hodgkin and Reed-Sternberg (HRS) cells. New targeted therapies for HL are warranted, especially for refractory/relapsed patients and elderly patients where limiting treatment toxicity is essential. CD83 is a member of the Ig superfamily that is expressed as a membrane molecule (mCD83) and as a membrane cleaved soluble molecule (sCD83). Our group reported that Hodgkin lymphoma tumor cells expressed mCD83 and sCD83 can be detected in serum in lymphoma patients. CD83 was identified as one of the four classifiers to distinguish HL with ALK-anaplastic large cell lymphoma. Despite its potential as a relatively specific target and potential biomarker, CD83 has not been investigated as a therapeutic target on HL.

Aims: The aim of this study is to assess whether CD83 is a potential biomarker and therapeutic target in HL patients. We developed a therapeutic human anti-human CD83 mAb, 3C12C, and its toxin conjugate, 3C12C-MMAE. We will test the killing efficiency of 3C12C and 3C12C-MMAE on HL cell lines. To “de-risk” the antibodies before advancing 3C12C into a clinical trial, we performed dose-escalation studies of 3C12C in non-human primates (NHP).

Methods: Immunohistochemical (IHC) staining of CD83 was performed on formalin fixed paraffin embedded (FFPE) lymph node biopsies of 35 HL patients. Serum samples were collected from HL patients at diagnosis and during sequential standard chemotherapy. Human scCD83 was analyzed by scCD83 ELISA kit. Antibody-dependent cell-mediated cytotoxicity (ADCC) was tested on HL lines using 3C12C mAb. 3C12C-toxin conjugate was prepared and tested for killing effect in vitro. For dose-escalation studies, five NHP received intravenous human-IgG or 3C12C mAb at days 0, 7, 14 and 21. PBMC were collected and analyzed for immune cell populations including DC, T and B cells on a Fortessa X20 flow cytometer. Liver and kidney function were assessed by measuring alkaline phosphatase (ALP), aspartate transaminase (AST) & creatinine in serum samples.

Results: IHC staining of HL patient FFPE biopsy samples showed 8/35 expressed high levels (10-90% positive) of CD83 on
the HRS cells (>90% positive), 21/35 expressed middle level and 6/35 expressed low levels (<10% positive) of CD83 (Fig1A). HL patients had significantly higher serum sCD83 (360.5±54.82 pg/ml, n=10) at diagnosis than healthy donors (52.6±9.5 pg/ml). High levels of sCD83 returned to normal in patients who had good clinical responses to chemotherapy confirmed by positron emission tomography scans (Fig1B). The ADCC activity of 3C12C was tested on the three HL lines: KM-H2, L428 and HDLM2. Whilst 3C12C killed KM-H2 and L428 efficiently, HDLM2 was relatively resistant to it (Fig1C).

To investigate further potential therapeutic applications, we generated a 3C12C toxin conjugate 3C12C-MMAE. 3C12C-MMAE killed CD83+ KM-H2 cells most efficiently, followed by HDLM2 and L428, while CD83- HL-60 cells were least sensitive to 3C12C-MMAE (Fig1D). In NHP trial with 3C12C, no toxicity was observed but there was evidence of CD83 positive target cell depletion in lymph node.

**Conclusion:** Most HRS in HL LN biopsies were CD83+ and sCD83 may be a useful blood biomarker to monitor disease. Anti-CD83 mAb, 3C12C and its toxin conjugate, kill CD83+ HL cells in vitro. No toxicity was observed in 3C12C dose escalation NHP study. These data establish CD83 as a potential biomarker and therapeutic target in HL.

**Keywords:** Antibody targeting, Hodgkin's lymphoma, Lymphocyte, Targeted therapy

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**Dr Yun Trieu (presenting on behalf of Ziba Gandomkar)**

**The University of Sydney**

**The abnormal gist in the prior mammograms even without visible cancer sign**

**ABSTRACT**

Can radiologists distinguish prior mammograms with no overt signs of cancer from women who were later diagnosed with breast cancer from the prior mammograms of women reported as normal and subsequently confirmed to be cancer-free? Twenty-three radiologists viewed 200 mammograms for a half-second and rated whether the woman would be recalled on a scale of 0 (clearly normal) to 100 (clearly abnormal). The dataset included five categories of mammograms, with each category containing 40 cases. The categories were Cancer (current cancer-containing mammograms), Prior-Vis (prior mammograms with visible cancer signs), Contra (current ‘normal’ mammograms contralateral to the cancer), Prior-Invis (priors without visible cancer signs), and Normal (priors of normal cases). For each radiologist, four pairs of analyses were performed to evaluate whether the radiologists could distinguish mammograms in each category from the normal mammograms: Cancer/Normal, Prior-Vis/Normal, Contra/Normal, and Prior-Invis/Normal. The Area under Receiver Operating Characteristic curves (AUC) was calculated for each paired grouping and each radiologist. Wilcoxon test showed the AUC values were above-chance for all comparisons (p<0.001). Therefore, radiologists can distinguish patients who were diagnosed with cancer from individuals without breast cancer at an above-chance level based on a half-second glimpse of mammogram even before the lesion becomes apparently visible.

**BIOGRAPHY of Ziba Gandomkar**

I have been working as a Research Associate at the University of Sydney since 2013 in the field of computer-assisted analysis of the mammograms, breast histopathological images, and low dose chest CT. I started my PhD in March 2015 at the University of Sydney. My PhD project deals with computer-assisted analysis of Hematoxylin-Eosin stained breast histopathological digital slides.

**BIOGRAPHY of Yun Trieu**

Yun Trieu graduated Bachelor of Medical Imaging at the University of Medicine and Pharmacy in Ho Chi Minh City in 2008. She became a student of the University of Sydney from 2011. Yun graduated Master course of Diagnostic Radiography in 2013 and completed the PhD in Health Sciences in 2017. Yun is a member of the Medical Image Optimization and Perception Research Group and she is currently doing postdoc research of the BreastScreen Reader Assessment Strategy at the University of Sydney. Her research focuses on risk factors for breast cancer and improving early breast cancer detection on medical images.
**Jarem Edwards**  
Melanoma Institute Australia  
*The Landscape of immune checkpoint receptors in untreated human melanoma*

**ABSTRACT**

**Introduction:** The introduction of anti-CTLA-4 and anti-PD-1 antibodies has had a profound effect on the treatment of advanced metastatic melanoma disease. Despite this, the majority of patients either fail to respond or acquire resistance to the therapy. In an attempt to address this clinical need, a number of new monoclonal antibodies targeting costimulating/coinhibitory receptors have entered clinical trials at our own Melanoma Institute of Australia and around the world. In this context, it is becoming increasingly important that oncologists and immunologists alike have an understanding of the basal frequency of these receptors in melanoma, how they change during normal progression of melanoma disease, and what immune populations are enriched for each of these checkpoints in the tumour.

**Methods:** Multifluorescence IHC staining for immune checkpoint receptors (ICOS, GITR, OX40, PD-1, TIM-3, VISTA, and LAG-3) was performed on a cohort of 44 melanoma patients with matching biopsies for primary, lymph node or distant metastasis. Mass cytometry was performed on TILs isolated from 5 untreated melanoma tumours.

**Results:** Multifluorescence IHC staining revealed that the ICOS costimulatory receptor was the most abundant checkpoint receptor in melanoma followed by PD-1, VISTA and other coinhibitory receptors. GITR and OX40 co-stimulators were the least abundant (approximately 10-15 fold less) of all the checkpoint receptors. Colocalization for each marker and CD3 on the same specimens revealed ICOS, PD-1 and GITR to be largely T cell specific, while the majority of TIM-3, VISTA, and OX40 positive staining were on non-T cell populations. Analysis between matched primary and distant metastatic melanoma in patients revealed no pattern of expression for the receptors, except for CD3+ GITR+ cells, which showed a significant decrease in density from primary to metastatic melanoma. Lastly, we performed Mass cytometry on TILs dissociated from untreated melanoma tumours to assess the various immune populations enriched for each of these receptors.

**Conclusion:** Our results provide oncoimmunologists a step forward to understanding the immune checkpoint landscape in melanoma, which will help them make better inferences on what patients will respond and how they might respond to each of the various therapies.

**BIOGRAPHY** Jarem is currently affiliated with both The Melanoma Institute of Australia and The Centenary Institute. He is currently doing his PhD in the field of Immuno-oncology with a particular emphasis on immunotherapy in melanoma. Jarem completed his Bachelor of Science (Advanced) with Honours Class I with the University Medal from the University of Sydney in 2016.

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**Dr Jolyn Hersch**  
The University of Sydney  
*Clinicians’ perspectives on Ductal Carcinoma In Situ (DCIS) among older women: a qualitative study*

**ABSTRACT**

DCIS incidence has increased greatly since the introduction of mammographic screening. As DCIS encompasses a spectrum of disease, including indolent lesions that may not progress, there is growing concern about overdiagnosis and overtreatment. The target age group for screening now includes women aged 70-74 whose potential for benefit and harm may differ from younger women.

**Methods:** We interviewed 26 clinicians (surgeons, radiation oncologists, breast physicians and nurses) working with DCIS patients in Australia/New Zealand. Interviews explored current practice and future directions for managing DCIS, patient communication issues, and benefits and harms of screening older women. Interviews were audio-recorded, transcribed, and analysed thematically.

**Results:** Many participants considered the screening age extension to be justified given increasing life expectancy in the population. On the other hand, many believed continuation of screening should depend on individual life expectancy given potential harms (e.g. overdiagnosis and overtreatment of low-grade DCIS among women in poor health). Some participants emphasised that women should be involved in making informed decisions about whether to screen.

**Discussion:** Doctors and nurses working with DCIS patients offer a valuable perspective on current issues around detection and management of DCIS. We will discuss key findings and implications for research, screening and clinical practice.

**BIOGRAPHY** Jolyn Hersch is a postdoctoral researcher at The University of Sydney School of Public Health, supported by an NHMRC Early Career Fellowship. Jolyn’s research aims to improve health communication to support people in making better informed health decisions that are consistent with their personal values. During and since her PhD, Jolyn has led a landmark RCT with longitudinal quantitative and qualitative follow-up, examining how information about overdiagnosis influences women’s decision making about breast cancer screening. Her postdoctoral project focuses on the under-researched topic of communication and decision making around managing screen-detected low-risk ductal carcinoma in situ.
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