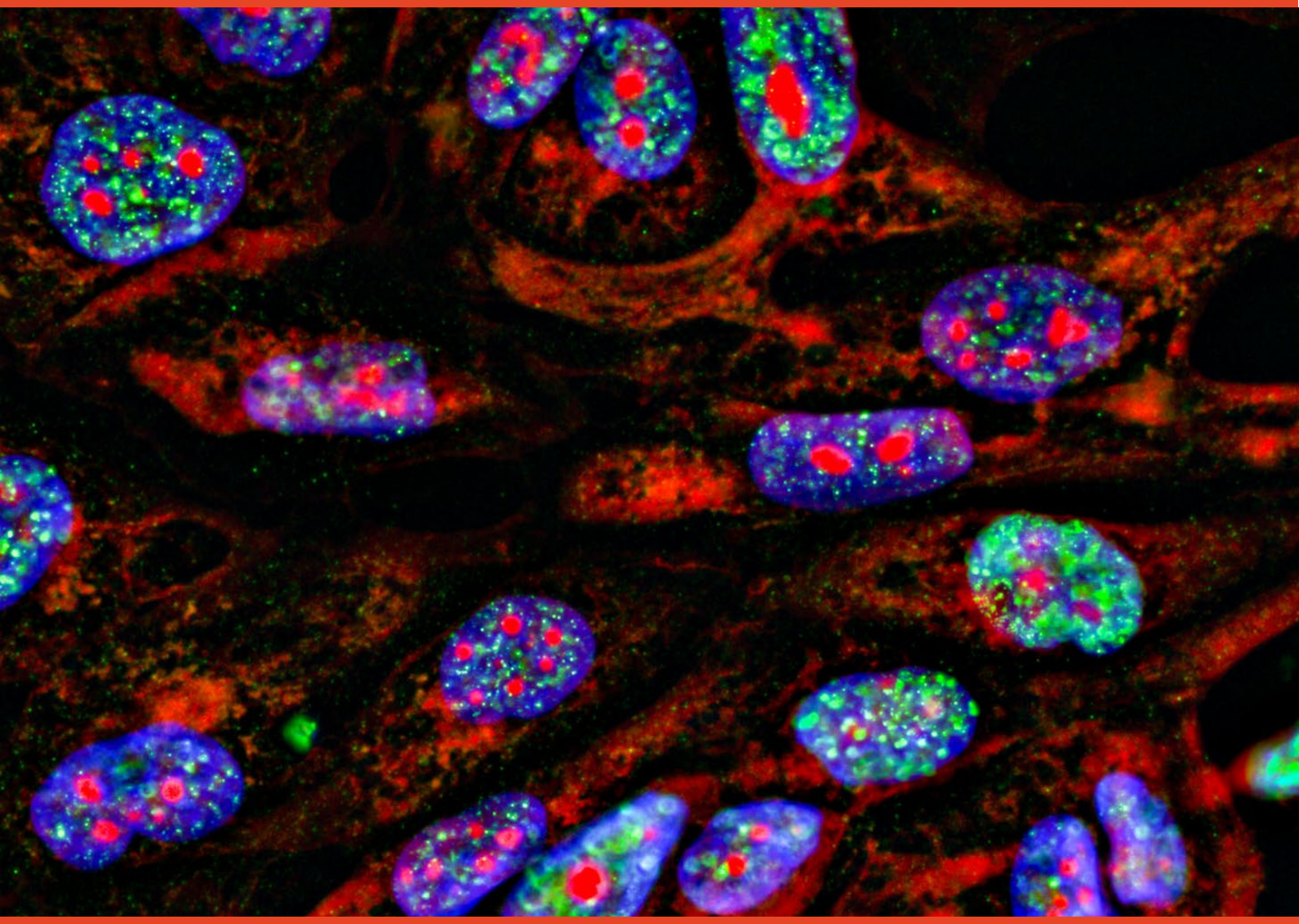
The Cancer Research Network presents the: 2022 POSTGRADUATE STUDENT CANCER RESEARCH SYMPOSIUM

17 November 2022



THE UNIVERSITY OF SYDNEY

Sydney Cancer Partners
Collaboration, Translation, Impact

2022 Postgraduate Student Cancer Research Symposium

CONTENTS:

About the Cancer Research Network

Established in 2006, the Cancer Research Network is a cross-Faculty initiative linking cancer researchers at the University of Sydney, its teaching hospitals and its affiliated research institutes and institutions. It encompasses a wide range of researchers who share a commitment to cancer research, collaborative research and research development. Our core values include a willingness to collaborate and share expertise, openness to multiple disciplines, and an interest in the translation of research findings into improvements in cancer control. The Network's membership has grown to over 1,000 active cancer researchers.

The Network fosters communication with and among members to facilitate multidisciplinary collaboration across research groups, with an emphasis on research translation. This builds a sense of community among cancer researchers across discipline and geographical boundaries.

The Network adapts and responds to the needs of cancer researchers, and through its activities stimulates knowledge transfer within the Network, the University and to the Government and public.

Membership is open to employees and postgraduate research students of the University of Sydney, people employed by teaching hospitals and Institutes of the University of Sydney, or people holding an academic title award from the University of Sydney, who are active in the area of cancer research.

For further information, please contact the Cancer Research Network Office

crn.cancer-research@sydney.edu.au
sydney.edu.au/cancer-research-network/

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Welcome message from the Symposium Chairs

On behalf of the Postgraduate Student Working Group (PGSWG) of the University of Sydney Cancer Research Network, we'd like to extend a warm welcome to the 14th Annual Postgraduate Student Cancer Research Symposium.

The Cancer Research Network represents cancer research students and academics across the University of Sydney, providing opportunities for networking and collaboration with like-minded colleagues. We are delighted to collaborate with Sydney Cancer Partners (SCP) again to make this symposium possible.

Thank you very much to every student who submitted abstracts - for your willingness to share your research and to support this year's symposium. We are delighted to have received so many submissions and registrations. This year's symposium focuses on the significance of translational research and its incorporation into the real world to create positive impacts in communities. Cancer researchers will present work that span across the translational research pipeline, from genomics and molecular biology to quality of life and survivorship.

We would also like to thank our wonderful keynote speakers Dr Brooke Nickel & Dr Jessamy Tiffen, and our panel speakers - A/Prof Natalie Taylor, Dr Felix Marsh-Wakefield, Dr Anna Singleton, Dr Tuba Nur Gide & Rachel Farber. We look forward to hearing from you all and will no doubt gain much inspiration and knowledge from what you have to share.

On behalf of the PGSWG, we would also like to extend our thanks to Marcel Batten and Jade Lor-Chan for their continued and unwavering support for this committee and event. A huge thank you must also go to all the members of the PGSWG who have put in so much time and energy to organise this year's events which would not be possible without their tremendous contributions!

We hope that you are inspired by each other and enjoy learning about all the amazing work going on through the CRN and beyond. Please engage with your colleagues and build new connections through Twitter by using #CRN2022Symposium and following us on @SydCancerNetwrk and @SydCancerPtnrs.

Jenna Smith, Vickie Chan

Co-chairs, Postgraduate Student Working Group (PGSWG)
Cancer Research Network

Keynote Speakers

Dr Brooke Nickel

NHMRC Emerging Leader Research Fellow
Sydney Health Literacy Lab
Sydney School of Public Health

Dr Brooke Nickel is a NHMRC Emerging Leader Research Fellow in the Sydney Health Literacy Lab in the University of Sydney School of Public Health.

Her research focuses on understanding the psychosocial impact of cancer diagnosis and treatment, and how to improve cancer communication and decision making. Her world-first research examines how different labels for low risk thyroid cancer impacts decision making and patient outcomes including quality of life.

Dr Nickel's work has been published in high impact journals in the field including The BMJ, JAMA Network Open, JAMA Otolaryngology-Head & Neck Surgery, and JNCI. She is currently working with the Department of Health and BreastScreen services on research related to understanding the benefits and harms of breast density notification in Australia.

Dr Jessamy Tiffen

Group Leader
Melanoma Epigenetics Lab
Centenary Institute of Cancer Medicine & Cell Biology

Dr Jessamy Tiffen is an Honorary Senior Research Fellow at the University of Sydney and a member of the Scientific Faculty at the Centenary Institute leading the Melanoma Epigenetics Laboratory.

Her lab focuses mainly on how dysregulation of epigenetic modifiers can govern major hallmarks of melanoma, including initiation, progression, and resistance to treatment. Dr Tiffen is passionate to determine the crosstalk between histone modifiers, chromatin remodelling enzymes and DNA methyltransferases in normal physiology and disease development. She aims to provide new insights into these fundamental biological mechanisms, which can be targeted by novel therapeutics to improve outcomes for melanoma patients.

She also has an excellent publication record and citations in high impact factor journals including Nature Genetics, Lancet Oncology, JNCI and Cancer Research. She currently holds funding from the Cancer Council of NSW and was awarded a Career Development Fellowship of the Cancer Institute of NSW earlier this year.

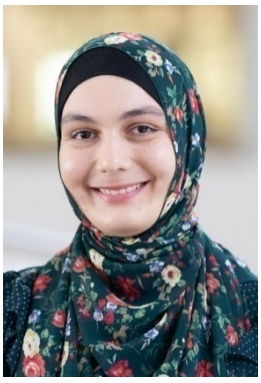
Panel Speakers

A/Prof Natalie Taylor

A/Prof Taylor is an implementation scientist who works on developing, applying, and advancing methods to support and study optimal ways to translate evidence into practice to improve care and outcome for patients. As the Director of Research in the School of Population Health at UNSW, she develops and enacts a research strategy for the school with a team of multidisciplinary academics, clinicians and professional staff. Her methodologies have been applied to a range of real-world problems and innovations, resulting in significant and sustained improvements in care and reductions in adverse events. This includes designing and evaluating an evidence-based framework for the implementation of patient safety guidelines in the NHS, as well as an intervention and training package for the prevention of childhood obesity.

Dr Felix Marsh-Wakefield

Dr Marsh-Wakefield is a post-doctoral researcher and immunologist, part of the Liver Injury & Cancer (Centenary Institute) and Human Cancer & Viral Immunology Laboratory (University of Sydney). He investigates the role of various immune cells in a range of diseases, including hepatocellular carcinoma and multiple sclerosis. This primarily involves bioinformatics to assist the analysis of high dimensional data, including that of imaging mass cytometry. Felix was awarded his PhD in 2018 at the University of Sydney, where he investigated the ability of mast cells to activate regulatory B cells. This involved the use of high dimensional cytometry, particularly mass cytometry, skills which were applied in his first post-doc.



Dr Tuba Nur Gide

Dr Gide is a post-doctoral researcher and recipient of the 2021 Early Career Fellowship grant at the Cancer Institute NSW. Her research, which is a continuation of her PhD studies, aims to identify which patients will respond to immunotherapy and those would benefit from an alternative treatment. This includes developing a panel of predictive tests using the clinical factors of the patient and different properties of tumours. The accuracy and benefit of the test to patients with advanced cancer will also be assessed to determine whether a reduction in drug-related side effects for the patient and costs to the health care system can be achieved.

Rachel Farber

Rachel Farber is a Senior Epidemiologist in the Centre for Epidemiology and Evidence at the Ministry of Health. Her work centres around Chief Health Officer projects with a focus on cardiac care. Her PhD was on the impacts of the change in technology in mammography screening. Rachel has taught epidemiology for almost a decade and is enthusiastic about collaborating on epidemiological methods.

Dr Anna Singleton

Dr Anna Singleton is an early-career researcher (PhD Dec 2021, MSc Experimental Psych; BSc Hons I Psych) and research fellow at the University of Sydney. Dr Singleton has won >270K in prizes and awards for her research and publications including$80K as CIA. In the last 5 years, she has 23 published peer-reviewed manuscripts (8 first-author, 1 senior-author), with many in high-ranking journals such as Journal of Clinical Oncology (IF 44.54), BMC Cancer, and JMIR. Dr Singleton's research focuses on using digital health strategies to support the health of cancer survivors, with the ultimate goal of lowering risks factors for cardiovascular disease and cancer recurrence.

PROGRAM

2022 STUDENT CANCER RESEARCH SYMPOSIUM

Thursday, 17 November 2022

Susan Wakil Health Building, The University of Sydney

	PLENARY SESSION ***Susan Wakil Health Building*** ***Level 3, Room 320*** **Chairs:** Vickie Chan, Jenna Smith		
8.30	Welcome and introduction		
8.35	**Keynote speaker 1** Dr Brooke Nickel "PhD to ECR – successes, failures, and (*trying to have*) impactful research..."		
9.05	Q & A		
CONCURRENT SESSIONS			
	Session 1a – Public health and psychosocial research (G1) *Level 3, Room 309* **Chairs:** Candice Donnelly & Madeleine Juhrmann	**Session 1b – Cell Biology, molecular biology and biomarkers (G1)** *Level 3, Room 320* **Chairs:** Sooin Byeon & Gemma Wilson	**Session 1c – Cancer treatments** *Level 3, Room 322* Chair: Miguel Castaneda
9.20	**1. The geography of prostate specific antigen testing in Australia: spatial analyses of Medicare claims data.** Ankur Kohar *The Daffodil Centre*	**5. Computational interrogation of telomere length and association with prostate cancer ethnic disparity** Ruotian Huang *Ancestry & Health Genomics Laboratory*	**9. Investigating the Course of Chemotherapy-Induced Neurotoxicity Over Time in Cancer Survivors** Tiffany Li *Brain and Mind Centre*
9.35	**2. Fear of cancer recurrence in ovarian cancer caregivers: A qualitative study** Kyra Webb *Psycho-Oncology Co-operative Research Group (PoCoG)*	**6. Pro-malignant interactions between clones in head and neck squamous cell carcinomas** Natnicha Ketchaikosol *Centre of Inflammation, Centenary Institute- UTS*	**10. The characterisation and impact of painful neuropathy phenotype in neurotoxic chemotherapy-treated patients** Fawaz Mahfouz *Brain and Mind Centre*
9.50	**3. Implementation of Geriatric Assessments in Cancer Care: An Umbrella Review** Sharon He *Psycho-Oncology Co-operative Research Group (PoCoG)*	**7. Designing a novel gene-editing strategy to combat TERT-specific telomere biology disorders** Lei He *Children's Medical Research Institute*	**11. Bone suppression and grayscale inversion improves lung nodule visibility on chest radiographs** Jessica Yi *Discipline of Medical Radiation Sciences*
10.05	**4. Systematic review of blended therapy interventions for the treatment of psychological disorders in adult patients: a background study for BT implementation research in Psycho-oncology in Australia** Kelly Nunes-Zlotkowski *Centre For Medical Psychology & Evidence-Based Decision Making (CMPED), Psycho-Oncology Co-operative Research Group (PoCoG)*	**8. Detecting Cancer-Associated Macrophage-Like Cells in Cancer Patients using the RareCyte Platform** Anthony Pirrello *Li Ka Shing Cell & Gene Therapy Program*	**12. Ketogenic diet combined with fasting as an adjuvant therapy in acute leukemia patients to reduce chemotoxicity and cellular damage.** Gayathiri Rajakumar *Nepean Clinical School*
10.20			**13. Targeting Mitochondrial Metabolism and Tumour hypoxia as an approach to Improve the Radiation Response in Diffuse Midline Gliomas** Faiqa Mudassar *Westmead Institute of Medical Research*
10.35	**MORNING TEA**		
CONCURRENT SESSIONS			

	Session 2a – Cell Biology, molecular biology and biomarkers (G2) *Level 3, Room 309* **Chairs:** Xinyu (Cath) Bai & Vickie Chan	**Session 2b – Cancer treatments + Anti-cancer agents and drug development** *Level 3, Room 320* **Chairs:** Tiffany Li & Katie McFadden	**Session 2c – Cell Biology, molecular biology and biomarkers (G3)** *Level 3, Room 322* Chair: Gemma Wilson & Miguel Castaneda
11.00	**14. Investigation of a novel therapeutic mechanism in aggressive leukaemia** Carla Jenson *Kolling Institute of Medical Research*	**19. Development of Novel Autophagy Inhibitors Based Anti-Cancer Combination Therapy** Yomna Saleh *Kolling Institute of Medical Research*	**24. Spatial characterisation of the tumour immune microenvironment in primary and metastatic melanoma** Grace Attrill *Melanoma Institute of Australia*
11.15	**15. The Tumour Microenvironment in Keratinocyte Cancers from Immunosuppressed Patients** Dr Catherine Zilberg *Department of Dermatology, Royal Prince Alfred Hospital*	**20. Investigation of a novel drug candidate for human uveal melanoma** Sebastian Liau *Sydney Pharmacy School*	**25. The role of metabolic stress in post-radiation tumour remodelling in human oral squamous carcinoma** Rabia Zafar *School of Medical Sciences*
11.30	**16. Personalising Novel Combination Immunotherapies for Advanced Stage Melanoma Patients** Ella McCutcheon *Melanoma Institute of Australia*	**21. Effects of [177Lu] Lu-PSMA-617 on overall survival in VISION versus TheraP randomized trials: An Exploratory Analysis** Yu Yang Soon *NHMRC Clinical Trial Center*	**26. Establishment of an in-vitro Extra-cellular matrix model and its effect on therapeutic response** Dr Maha Aman *Sydney Dental School*
11.45	**17. Biomarkers of Response and Resistance to Lenvatinib plus Anti-PD-1 in Advanced Melanoma** Alexander Siu *Melanoma Institute of Australia*	**22. CRISPR Based Knockout of HLA Class I and II to Prevent Allorejection of Off the Shelf Chimeric Antigen Receptor T-cells** Melanie Mach *Westmead Institute for Medical Research*	**27. Proteomic analysis of non-invasive biopsies of atopic dermatitis, psoriasis, and actinic keratosis for the identification of diagnostic biomarkers.** Lauren Faul *Westmead Institute for Medical Research*
12.00	**18. Investigating predictive biomarkers in adjuvant immunotherapy for stage III melanoma patients** Michael Xie *Melanoma Institute of Australia*	**23. A Computational Investigation to the Radiobiological Effects of Secondary Particles in Scanning Beam Proton Therapy** Michael Lloyd *Institute of Medical Physics*	**28. C-circle testing as an 'ALT'ernative Liquid Biopsy approach for Osteosarcoma** Ella Rose Dopper *Children's Cancer Research Unit*
12.30	**LUNCH**		
1.30	**Panel discussion** ***Susan Wakil Health Building, Level 3, Room 320*** **"Surviving in Science: Transition and Translation"** **Chairs:** Ruth Allen & Rebecca Simpson **Panel Members:** A/Prof Natalie Taylor, Dr Felix Marsh-Wakefield, Dr Anna Singleton, Dr Tuba Gide, Rachel Farber		
CONCURRENT SESSIONS			
	Session 3a – Cell Biology, molecular biology and biomarkers (G4) *Level 3, Room 309* **Chairs:** Nancy Santiappillai & Miguel Castaneda	**Session 3b – Clinical research** *Level 3, Room 320* **Chairs:** Tiffany Li & Kyra Webb	**Session 3c – Public health and psychosocial research (G2)** *Level 3, Room 322* Chair: Jenna Smith & Gillian Reyes-Marcelino
2.15	**29. Better Models for Better Breast Cancer Research: Could 3D models of non-invasive breast cancer reveal the key to invasive progression?** Sarah McLucas *Westmead Institute for Medical Research*	**34. Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma: Clinical Outcomes by Genotype** Henry Crayton *Sydney Medical School*	**38. A review of mental health services in the diagnostic journey of cancer patients** Kelera Levu *Brain and Mind Centre*
2.30	**30. Cracking the genomic puzzle of paediatric cancer predisposition** Safaa Al Haj Hussein *Children's Hospital at Westmead Clinical School, Kids Research Institute (KRI)*	**35. Frequency and Characteristics of Errors performed by Artificial Intelligence in Reading Screening Mammography: A Systematic Review** Aileen Zeng *Daffodil Centre*	**39. Factors associated with psychosocial impacts of lung cancer screening: a systematic review** Kathleen McFadden *Daffodil Centre*
2.45	**31. Neurofilament Light Chain in Axonal Degeneration in**	**36. Methods for dealing with missing outcome data in randomised**	**40. Prevalence of Epstein-Barr virus infection in China: a cross-sectional study**

	Chemotherapy Induced Peripheral Neurotoxicity Masarra Al Deleemy *Brain and Mind Centre*	**controlled trials: a methodological scoping review** Ellie Medcalf *Sydney School of Public Health*	Xintong Huang *Faculty of Medicine and Health*
3.00	**32. Detection and analysis of wrongly identified nucleotide sequence reagents in high impact factor cancer research journals** Pranujan Pathmendra *Marie Bashir Institute*	**37. Serum Metallome of Pancreatic Ductal Adenocarcinoma** Sooin Byeon *Kolling Institute of Medical Research*	**41. A systematic review of dentists' perceptions and practices towards dental care management in patients undergoing cancer therapies** Dr Sheau Ling Low *School of Psychology*
3.15	**33. Machine learning-based proteomic prediction of squamous cell carcinoma subtype from 80 cancer cell lines** Dr Emma Boys *Children's Medical Research Institute*		**42. The impact of adopting the Anticancer Drug Dosing in Kidney Dysfunction guideline on Carboplatin dosing** Matthew Ghobrial *Sydney Pharmacy School*
3.30	**AFTERNOON TEA**		
3.45	**Keynote speaker 2** ***Susan Wakil Health Building, Level 3, Room 320*** Dr Jessamy Tiffen "A Career in Cancer Research: Riding the highs and surviving the lows" **Chairs:** Vickie Chan and Jenna Smith		
4.15	Q & A		
	AWARDS & CLOSING CEREMONY ***Susan Wakil Health Building, Level 3, Room 320*** **Chairs:** Vickie Chan, Jenna Smith		
4.30	Most outstanding student presenter within each of the following sessions: • Public health and psychosocial research (x2) • Cell Biology, molecular biology and biomarkers (x4) • Cancer treatments and anti-cancer agents and drug development (x2) • Clinical research		
4.45	**FINISH**		
5.00-6.00	**Networking Drinks & Canapes** *Susan Wakil Health Building, Level 4 Foyer*		

ABSTRACTS

Session 1a: Public health and psychosocial research

1. The geography of prostate specific antigen testing in Australia: spatial analyses of Medicare claims data

Ankur Kohar* (1, 2), Susanna M Cramb (3, 4, 5), Kristen Pickles (6), David P Smith (1, 7), Peter D Baade (8, 3, 9)

(1) The Daffodil Centre, The University of Sydney, a joint venture with Cancer Council NSW, Sydney, New South Wales, Australia.
(2) Sydney School of Public Health, The University of Sydney
(3) Centre for Data Science, Faculty of Science, QUT, Brisbane, Australia
(4) School of Public Health and Social Work, Queensland University of Technology, Brisbane, Australia
(5) Australian Centre for Health Services Innovation & Centre for Healthcare Transformation, Queensland University of Technology, Brisbane, Australia
(6) Faculty of Medicine and Health, Sydney Health Literacy Lab, School of Public Health, The University of Sydney, Sydney, Australia
(7) School of Public Health and Preventive Medicine, Monash University, Melbourne, Victoria, Australia.
(8) Cancer Council Queensland, Brisbane, Australia
(9) Menzies Health Institute, Griffith University, Gold Coast, Australia

Background: Prostate-specific antigen (PSA) testing rates in Australia vary by socio-economic status and remoteness, although little is known about the level of variation within these broad groups.

Aim: This population-based cohort study aims to quantify the small area geographical variation in PSA testing rates across Australia.

Methods: The Commonwealth Department of Health provided Medicare Benefits Schedule (MBS) data for PSA "screening" tests (MBS Item number 66555) for all reimbursed tests in Australia in 2017 and 2018. A probability-based concordance using 50-iterations was used to map each postcode of residence of men tested to a small areas (Statistical Areas 2; n=2,129). Standardised Incidence Ratios (SIRs) were smoothed (by borrowing information from neighbouring geographical areas) using a Bayesian spatial Leroux model, and estimates were averaged across all iterations.

Results: There were 925,079 (26% of the male population) men aged 50-79 years with a record of a PSA test during 2017-18, giving an overall crude "screening" rate of 260.6 per 1000 men. The screening rates varied 20-fold among small areas. Screening rates were higher (exceedance probability>0.8) than the Australian average in the majority of small areas in southern Victoria, South Australia, south-west Queensland and some coastal regions of Western Australia. PSA screening rates were lower (exceedance probability<0.2) in most small areas in Tasmania and the Northern Territory compared to the national average.

Summary/Conclusion: This study demonstrates the considerable geographical variation in use of PSA testing across small areas in Australia. Differences in access to and guidance provided by clinicians, and behaviour and preferences of men could influence variation in screening rates. Greater understanding of geographical PSA testing patterns by small areas and their associations to health outcomes can inform evidence-based approaches to identify and manage prostate cancer risk.

Presenter Bio:
Ankur is a PhD candidate at the University of Sydney, with a strong background in mathematics and statistics. His main research interests are cancer epidemiology and disease mapping, and he has collaborated on these with The Daffodil Centre. His PhD is investigating geographic and temporal variation in PSA screening across Australia. Ankur is an affiliate member of the NHMRC Centre for Research Excellence in Prostate Cancer Survivorship (CRE-PCS) and supported by a combined scholarship from Australian Rotary Health and The Daffodil Centre.

2. Fear of cancer recurrence in ovarian cancer caregivers: a qualitative study

Kyra Webb*(1), Louise Sharpe (1), Hayley Russell (2) and Joanne Shaw (1, 3)

(1) School of Psychology, Faculty of Science, The University of Sydney
(2) Ovarian Cancer Australia
(3) The Psycho-oncology Co-operative Research Group (PoCoG), School of Psychology, Faculty of Science, The University of Sydney

Aims: Fear of cancer recurrence or progression (FCR) is reported in 50% of people with ovarian cancer. Whilst research exploring patient FCR has increased, little is known about caregiver FCR. To date caregiver research has been conducted through the prism of patient conceptualisations, limiting the development of models, measures and interventions which are specific to caregivers. The aim of this study was to explore experiences of FCR in ovarian cancer caregivers.

Methods: Semi-structured telephone interviews were conducted with caregivers of people with ovarian cancer. Participants were recruited through Ovarian Cancer Australia and also completed a short online survey collecting participant and patient demographic characteristics, information about the patient's disease and caregiver levels of FCR using the Fear of Cancer Recurrence Inventory (Caregiver) (FCRI-c). Interviews explored caregiver fears, how the fears and worries were experienced and the frequency and timing of FCR. Thematic analysis was used to analyse the results.

Results: 24 caregivers (54% male) participated in an interview. Most caregivers were providing care for their partner (n = 14). Thematic analysis revealed four inter-related themes and additional sub-themes: 1) Fear and worry; 2) Liminality; 3) Hopelessness and 4) Caregiver's role as protector. An overarching theme, fear of one's family member dying underpinned each theme. The protector role was dual in nature and functioned to protect both the patient and caregiver, explaining different behaviours.

Conclusions: Aspects of FCR unique to the caregiver were identified. Caregivers are also impacted by fears and concerns of cancer recurrence or progression. In the context of ovarian cancer, caregiver FCR experiences differ conceptually from those reported by patients. Caregivers play a vital role in supporting people with ovarian cancer. Further research is critical to determine whether caregiver FCR is conceptually similar across cancer types. This research is the first step in the development of interventions tailored to caregiver needs.

Presenter Bio:
Kyra Webb is an early career researcher focusing on psycho-oncology. She holds a Bachelor of Psychological Science (Hons) and is a PhD candidate and Research Assistant in the School of Psychology, at The University of Sydney. Her early-career work focuses on caregiver experiences of fear of cancer recurrence (FCR), examining differences between existing patient models of FCR and caregiver experiences. Kyra is passionate about contributing to evidence-based resources which support caregivers, a group providing substantial assistance and support to cancer patients.

3. Implementation of Geriatric Assessments in Cancer Care: An Umbrella Review

Sharon He* (1) , Heather Shepherd (2) , Meera Agar (3) , Joanne Shaw (1)

(1) School of Psychology, Faculty of Science, The University of Sydney, Camperdown, NSW, Australia
(2) Susan Wakil School of Nursing and Midwifery, Faculty of Medicine and Health, The University of Sydney, Camperdown, NSW, Australia
(3) Improving Palliative, Aged and Chronic Care through Clinical Research and Translation (IMPACCT), Faculty of Health, University of Technology Sydney, Ultimo, NSW, Australia

Background: Geriatric assessments (GAs) can assist with identifying older cancer patients at risk of treatment complications and guide treatment decision-making, hence optimising outcomes for older cancer patients. However, there is uncertainty about what defines a GA in cancer care and the factors that impact on GA implementation in cancer settings.

Aim: The aim of this umbrella review was to summarise and synthesise the evidence for i) what constitutes a GA in cancer care, ii) how GAs are conducted, iii) which outcomes are used to assess the efficacy of GAs and iv) how implementation of GAs in oncology settings are reported.

Methods: PsycINFO, MEDLINE, Embase, CINAHL, Cochrane Library and Web of Science databases, were searched. Eligible reviews included systematic reviews with or without meta-analyses that i) described the use/ value of GA in cancer or ii) information related to implementation of GA in cancer settings. Two reviewers reviewed articles for eligibility; data was extracted, and quality appraisal was conducted. Review registration was PROSPERO:CRD42022338842.

Results: Of the 3,494 titles and abstracts screened, 128 full-text articles were reviewed, and 35 reviews were included in the umbrella review. Definitions of GA included interviews, multi-dimensional assessments to self-assessments. Most reviews reported that GAs were performed prior to treatment by patients themselves or by a range of health professionals (oncology team, physicians, nurses, and geriatricians). Reported outcomes included adverse treatment effects, specifically treatment toxicity and perioperative complications (24/35 reviews), mortality/survival (22/35), treatment modification (12/35), treatment adherence or completion (12/35) and resource-related outcomes (8/35). 8 reviews reported on the number and type of GA-based interventions. Only 5 reviews reported barriers and enablers to GA implementation and no reviews reported use of frameworks to guide GA implementation.

Conclusion: Implementation of GA as part of standard care in Australian cancer services requires clearly defined outcomes and care pathways.

Presenter Bio:
My PhD aims to explore and understand current Australian practice to inform the development of a consensus, evidence-based care pathway to identify and manage geriatric needs for older adults with cancer. I also aim to assess the feasibility and acceptability of implementing the care pathway for use in routine cancer care to optimise outcomes for older Australians with cancer.

4. Systematic review of blended therapy interventions for the treatment of psychological disorders in adult patients: a background study for BT implementation research in Psycho-oncology in Australia

Kelly Nunes-Zlotkowski* (1), Heather Shepherd (1), Phyllis Butow (1), Lisa Beatty (2), Joanne Shaw (1)

Lead Research Supervisor: A/Prof Joanne Shaw, joanne.shaw@sydney.edu.au
PhD student: Kelly Ferrao Nunes-Zlotkowski, kelly.nunes@sydney.edu.au
(1) Psycho-Oncology Co-operative Research Group, School of Psychology, The University of Sydney, Sydney, Australia
(2) Clinical Psychology, College of Education, Psychology and Social Work, Flinders University South Australia, Adelaide, Australia

Background: research suggests the efficacy and cost-effectiveness of blended psychological therapy (BT) in the cancer context. Blending online with face-to-face interventions provides an opportunity to increase access to treatment; to improve therapy uptake and adherence; to assist with treatment maintenance; and to boost therapy effects.

Aim: This systematic review synthesises the literature to investigate content and structure characteristics of digital and face-to-face components in BT.

Method: Following the PRISMA guidelines, we searched PsycINFO; CINAHL; EMBASE; ProQuest; MEDLINE databases using keywords and MeSH terms related to BT (e.g. 'blended'; 'face-to-face'; 'online'; 'psychological distress or disorder'). We screened articles published in English to May 2022 describing or applying interventions where digital and face-to-face elements were part of a treatment plan. Two researchers reviewed articles for eligibility, extracted data and conducted quality appraisals. Quantitative data were summarised and the structure and content of BT interventions categorised based on a coding framework. Qualitative data were thematically analysed. A systematic narrative synthesis explored the findings of included studies.

Results: Database searches identified 2927 studies. After removing duplicates, 2166 papers were title and abstract screened. Full text review of 84 articles resulted in 24 eligible papers. An updated search identified another four papers for inclusion. BT interventions' structure and content distribution were analysed and classified according to: i) mode of interaction between digital/face-to-face components; ii) role of the digital component in the treatment; iii) digital component mode of delivery and iv) digital materials assignment mode.

Conclusion: Based on key themes identified regarding interventions' structure and components, we propose a taxonomy for BT models. The proposed classification will assist with assessing and evaluating BT models in a subsequent study. Participants' feedback will underpin the development of a BT model for the treatment of anxiety and depression in adult cancer patients to be tested at Australian psycho-oncology services.

Presenter Bio:
This systematic review focussed on the identification, characterisation, and synthesis of the literature related to blended psychological therapy (BT). Specifically, this study aimed to investigate (i) blended therapy definition(s) described and applied for the treatment of psychological disorders in adult patients, and (ii) the structure, content and ratio of both online and face-to-face sessions described and applied in blended therapy models studied. Results of this review aim to inform the development of a future BT model for the treatment of anxiety and depression in cancer patients that would be feasible and acceptable for use in Australian psycho-oncology services.

Session 1b: Cell biology, molecular biology and biomarkers

5. Computational interrogation of telomere length and association with prostate cancer ethnic disparity

Ruotian Huang* (1), Weerachai Jaratledsiri (1), Vanessa M. Hayes (1)

(1) Ancestry & Health Genomics Laboratory, Charles Perkins Centre, School of Medical Sciences, Faculty of Health & Medicine, University of Sydney, Camperdown

Background. Telomere is a hexamer repeat motif, TTAGGG, at the 3' end of each chromosome preserving the genomic integrity and chromosomal stability. While telomere length (TL) has only recently been associated with genomic instability and clinical outcomes for prostate cancer (PCa), no study has explored the relationship between TL and PCa ethnic disparity, which places men of African ancestry at the greatest risk for aggressive disease. Additionally, TL has largely been ignored in whole genome sequencing (WGS) cancer landscaping studies as a direct result of the inherent difficulties in interrogating chromosome ends.

Aims. (1) To establish the reliability and validity of computational TL measurement techniques, TelSeq and Telomerecat. (2) To determine if TL is correlated with ethnic disparities in clinical presentation and genomic features in a unique cohort of African versus European PCa cases.

Methods. WGS tumour-blood paired PCa data from men of African (South Africa) versus European (Australia) ancestry (n=183), showing significant genomic disparity, was made available to this study. TL estimations were derived using TelSeq in triplicate and/or Telomerecat for five replicates each at Telbam generation and TL estimation. T-test was conducted between TL and other related variables in R.

Results. Comparing the methodologies, we found TelSeq generated stable TL estimates in all duplicated experiments, while no uniformity could be established using Telomerecat. Continuing with TelSeq, we identify a significant difference between the ethnicities and clinical presentation, with tumour TL (short/long) associated with aggressive disease in men of African ancestry. Conversely, TL ratio (Tumor/Blood) implied a correlation with tumour mutational burden in European men, and with percentage genome alteration in both ethnicities.

Summary. We show TelSeq to exceed Telomerecat in both accuracy and stability. For the first time, our study is alluding to a potential role for TL in driving PCa ethnic disparity.

Presenter Bio:
We aimed to establish the reliability and validity of computational TL measurement techniques, TelSeq and Telomerecat, and also other tools in further study. We also determined if TL is correlated with ethnic disparities in clinical presentation and genomic features in a unique cohort of African versus European PCa cases.

6. Pro-malignant interactions between clones in head and neck squamous cell carcinomas

Natnicha Ketchaikosol* et al

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(4) Dermatology, Royal Prince Alfred Hospital

Head and neck squamous cell carcinoma (HNSCCs) are the seventh most common cancer worldwide. Recent next-generation sequencing has revealed that HNSCCs often display genetic intratumoral heterogeneity, consisting of many subclones which have their own genetically unique characteristics. This raises the possibility that these clones could interact to enhance tumour initiation, invasiveness and progression. However, clonal interactions between HNSCC subpopulations have not been widely investigated.

The aim of this study is to identify pairs of HNSCC clones that can interact to promote cell proliferation, migration and tumorigenesis, and to identify the pathways that mediate those interactions.

CISCCO-02, a HNSCC cell line derived from Confetti mice undergoing 4NQO carcinogenesis, and human cell lines, including HN30, SCC9 and SCC25, will be investigated in this study. These cell lines were chosen because there is genetic and/or morphological evidence that they are multiclonal. To study the clonal interactions, each clone will be tagged with a distinctive fluorescent protein. Then they will be cultured individually and as a mixture, and cell proliferation, invasion and migration assays will be performed. Once interacting clones have been identified, the pathways which enable those interactions will be identified using a CRISPR lentiviral screen.

All of the mentioned cell lines have been cloned. Two clones, one cyan and one red, were selected from a Confetti mouse HNSCC cell line. Intravital imaging of the tumour that gave rise to the cell line showed that the cyan clone grew slowly until it was invaded by the adjacent red clone. HN30 and SCC9 clones stably maintain their epithelial and mesenchymal morphologies. These preliminary data showed that these HNSCC cell lines have dimorphic clones, and they could potentially interact to promote tumour progression. Nevertheless, the interactions between these clones remain to be investigated.

Presenter Bio:
NA

7. Designing a novel gene-editing strategy to combat TERT-specific telomere biology disorders

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Background:
Telomerase is an enzyme that can actively lengthen telomeres, which is an important molecular feature in normal stem cell physiology. Patients with hereditary mutations in TERT – the gene that encodes the telomerase catalytic subunit, usually develop bone marrow failure (BMF) due to proliferation defects in their haematopoietic stem cells. This study aims to develop a CRISPR-Cas9 gene editing strategy to form the pre-clinical foundation of a novel gene therapy targeting the TERT gene to combat BMF.

Methods:
CRISPR technology relies on the endonuclease Cas9 generating a double-strand break which is guided by a single guide RNA (sgRNA) targeting the specific genome location. We used two Cas9-sgRNA ribonucleoprotein complexes to cleave out the defective alleles and replace them with a functional gene copy via a viral AAV vector, a strategy known as Homology Independent Targeted Insertion (HITI). Our CRISPR-Cas9 HITI-2c approach was successful in targeting TERT. Flow cytometry analysis of GFP expression showed successful viral transduction in 63% of the modelled K562 cells. The top 10% of GFP+ cells were selected for sorting to be genotyped.

Results:
The FACS-sorted GFP+ population were found to successfully have been gene-edited in the TERT alleles. However, various insertions and deletions (indels) patterns and some AAV random viral integrations were also present. A CRISPR-HITI strategy via double-cut Cas9-gRNA RNP and AAV donor integration was found to yield ~50% successful donor integration events. It provided some pre-clinical evidence that this gene-editing approach could be applied to haematopoietic stem cells as an ex vivo gene therapy.

Conclusion:
Future directions would aim to minimise insertion/deletion rates and to optimise the gene editing efficiency, before efficacy testing in vivo in humanised-mouse models.

Presenter Bio:
NA

8. Detecting cancer-associated macrophage-like cells in cancer patients using the RareCyte Platform

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Background
Cancer-associated macrophage-like cells (CAMLs) traverse the peripheral blood of patients in all stages of cancer development and have been reported in many solid malignancies. Current methods to isolate these rare cells mainly use microfiltration techniques such as CellSieve. A density-based separation technology, RareCyte, provides cell-lossless isolation of peripheral blood mononuclear cells, whereby immunofluorescence staining and automated image analysis can identify potential cells of interest. To our knowledge, this is the first utilisation of the RareCyte platform to examine the prevalence of CAMLs in cancer patients.

Aim
To establish methods for CAML detection using the RareCyte platform.

Methods
Human pancreatic cancer cells, Capan-2, and differentiated THP-1 monocytes were spiked into 7.5 mL of healthy blood and processed on the RareCyte platform. Isolated cells were identified by a custom antibody panel comprising cytokeratin (CK), epithelial cell adhesion molecule (EpCAM), CD45, and CD14. Blood from an extensive-stage small cell lung cancer patient was analysed for circulating tumour cell (CTC) and CAML analysis.

Results
The RareCyte platform detected both spiked-in Capan-2 cells and differentiated THP-1 monocytes. In the cancer patient sample, 8 cells with CAML-like properties were identified along with 189 CTCs.

Conclusion
We have designed and optimised methods for concurrent CTC and CAML detection using the RareCyte platform. The analysis of additional cancer patient samples is planned, as well as the characterisation of the identified CAMLs using single-cell sequencing methods.

Presenter Bio:
My research has focused on capturing and analysing rare cells traversing the blood of cancer patients. Through this, we hope to better understand a patient's underlying cancer to identify effective therapies.

Session 1c: Cancer treatments

9. Investigating the Course of Chemotherapy-Induced Neurotoxicity Over Time in Cancer Survivors

Tiffany Li* (1), Hannah C. Timmins (1), Terry Trinh (2), Lisa G Horvath (3), Michelle Harrison (3), Peter Grimison (3), Matthew C. Kiernan (1), David Goldstein (2,4), Susanna B. Park (1)

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(3) Chris O'Brien Lifehouse, Australia
(4) Prince of Wales Hospital, Randwick, Australia

Background
Chemotherapy-induced peripheral neurotoxicity (CIPN) is a common side effect of neurotoxic cancer treatments producing numbness, tingling and pain in hands and feet. Although CIPN may persist for years post-treatment completion, little is known about CIPN outcomes in cancer survivors.

Aim
This study aimed to evaluate the trajectory of CIPN using clinical and neurological grading, patient reported outcome (PRO) and semi-objective sensory measures.

Method
Patients were recruited prior to commencing treatment with neurotoxic cancer treatment (taxanes, platinums, vinca-alkaloids, bortezomib, thalidomide) and assessed at three timepoints post-treatment completion (T1=3-4months, T2=6-8months, T3=15-25months post-treatment). Outcome measures included the National Cancer Institute sensory neuropathy scale (NCI, range 0-4), Total Neuropathy Score, clinical version (TNSc, range 0-24), sensory neuropathy PRO (CIPN8, range 0-100), and semi-objective sensory measures on the fingertips (grating orientation task (GOT, range 0.35-12mm), Von Frey monofilaments (VF, 0.125-512mN)). Assessment scores were assessed between timepoints using paired t-test. Results presented as mean±SD.

Results
163 patients (mean age 55.2±11.8years, 67.3% female) were assessed at all three timepoints, with 106 patients (65.0%) having developed CIPN of any grade by T1. There was significant improvement in mean NCI grade over time (P<0.001). Patient reported CIPN severity improved by T2 compared to T1 (CIPN8=21.2±15.8 vs 16.5±14.9, P<0.001), but remained stable at T3 (CIPN8= 16.6±15.9). On neurological grading scale (TNSc) and both semi-objective sensory measures, there was no improvement until T3 compared to T1 (TNSc= 3.8 ± 2.6 vs 4.7± 2.6, P<0.001, GOT= 3.7± 1.7mm vs 4.3± 2.5mm, P<0.01, VF= 0.4± 0.5mN vs 2.7 ± 10.4mN, P<0.05).

Conclusion
CIPN affected 65.0% of cancer survivors treated with neurotoxic treatment. Patient-reported symptoms improved by 6-8 months, but remained stable at later timepoints. In contrast, neurological and sensory tests did not show improvement until 15-25 months post-treatment, suggesting differences between patient perception and objective assessment of neurotoxicity.

Presenter Bio:
I am a third year postgraduate researcher investigating peripheral neurotoxicity following neurotoxic cancer treatments. Peripheral neurotoxicity is a common and debilitating side affect of various chemotherapy treatments. Despite this, there is currently still no treatment or preventions for this side affect. My research focusses on investigating the risk factors, phenotypes and outcome measures used in assessing chemotherapy-induced peripheral neurotoxicity.

10. The characterisation and impact of painful neuropathy phenotype in neurotoxic chemotherapy-treated patients

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(3) Department of Medical Oncology, Prince of Wales Hospital, Randwick NSW, 2031, Australia

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a common side-effect of neurotoxic chemotherapy treatment. Our understanding of the impact of different CIPN phenotypes on symptom severity and burden is limited. Furthermore, literature distinguishing between painful and non-painful CIPN phenotypes is scarce.

Aim: To identify differences in neuropathy phenotypes between painful and non-painful CIPN and investigate potential behavioural changes associated with the painful CIPN phenotype.

Methods: 597 participants (mean age=57.4±12.8 years; F=66%) were assessed cross-sectionally 5.5±3.1 months post-treatment. CIPN severity was graded using patient-reported outcome (EORTC-QLQ-CIPN20), a clinically-graded scale (NCI-CTCAE), and a neurological examination score (Total Neuropathy Score-clinical version (TNSc)). Participants were dichotomised into painful CIPN and non-painful CIPN groups according to the presence or absence of shooting/burning pain (EORTC-QLQ-CIPN20), while those in the non-painful CIPN group reported numbness or tingling without shooting/burning. Potential behavioural were assessed by structured patient interview questions regarding symptom impact on sleep, exercise and treatment-seeking behaviour and compared between patients with painful CIPN and non-painful CIPN.

Results: Among 579 participants, 24% (n=140) reported painful CIPN, 48% (n=280) reported non-painful CIPN and 28% (n=159) had no CIPN (excluded from further analyses). Participants with painful CIPN demonstrated higher severity of CIPN across multiple measures than participants with non-painful CIPN, including NCI-CTCAE, TNSc and EORTC-QLQ-CIPN20 (all p<0.05). Participants with painful CIPN were twice-as-likely to report that their symptoms affected their ability to exercise (p=0.007), and three-times-as-likely to report trouble sleeping as well as seeking treatment due to their symptoms (both p<0.001), in comparison to participants with non-painful CIPN.

Summary/Conclusion: Overall, participants with the painful CIPN phenotype reported higher scores across all CIPN severity measures, including behavioural changes to exercise, sleep, and treatment-seeking behaviour. This underlines the need for accurate identification of different CIPN phenotypes, in hopes of informing better treatment and rehabilitation options for cancer survivors with painful CIPN.

Presenter Bio:
My research centres around classifying chemotherapy-induced peripheral neuropathy (CIPN) pain responses by using neurophysiological techniques and by identifying accurate tools for the assessment of painful CIPN in the hopes of having personalised treatment and pain management for cancer patients.

11. Bone suppresion and grayscale inversion improves lung nodule visibility on chest radiographs

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Rationale and Objectives: To investigate the effect of bone suppression and grayscale inversion technology on the visualisation of lung nodules on chest radiographs. The influence of nodule size, radiodensity and tube voltage were also considered.

Materials and Methods: 180 experimental radiographs were acquired using a chest phantom and processed with bone suppression, grayscale inversion and a combination of the two. Each image had six synthetic nodules of two densities: +100 HU and -630 HU and three sizes: 12 mm, 10 mm and 8 mm, which were arranged within the phantom a total of five times to produce 30 locations. Visual grading analysis (VGA) was performed by an experienced reader to compare each nodule on the experimental images with the control using a five-point rating scale. Wilcoxon signed-rank test was used to analyse the VGA scores.

Results: Significant higher VGA scores (P = 0.034) were all recorded for 8 mm nodules with +100 HU at 102 and 125 kVp, and with -630 HU at 102 kVp when bone suppression was compared with the control. Grayscale inversion recorded enhancements for 8 mm nodules with +100 HU at 102 kVp (P = 0.038) and 125 kVp (P = 0.025), and for -630 HU at 102 kVp (P = 0.034). When bone suppression and grayscale inversion were combined, similar improvements were found for 8 mm nodules at 102 kVp (P = 0.025) and 125 kVp (P = 0.025) with +100 HU and at 102 kVp with -630 HU (P = 0.034) when rated against the control.

Conclusion: The visibility of small nodules and subsolid lesions were specifically improved through bone suppression, grayscale inversion and the combined use of the two. These technologies potentially enhance the diagnostic value of chest radiography as one of the most affordable and accessible forms of chest imaging.

Presenter Bio:
This study provides an original report on how the value of plain chest radiography can be potentially increased through the use of bone suppression and grayscale inversion in lung nodule detection. Pulmonary nodules are an indicator of lung cancer, where early detection of these lesions is essential. Plain chest radiography is the most available form of chest imaging and the first-line modality used in lung cancer investigation, however, they are associated with a high rate of error. Post-processing techniques such as bone suppression and grayscale inversion can enhance image quality and improve the detectability of cancerous nodules.

12. Ketogenic diet combined with fasting as an adjuvant therapy in acute leukemia patients to reduce chemotoxicity and cellular damage

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Background: One in three Australians are diagnosed with cancer- most are treated with chemotherapy. Most chemotherapies target rapid proliferating cells which means they kill both cancer and some healthy cells. Consequently, chemotherapy causes severe cellular damage to healthy tissues, manifesting as acute side effects and leading to chronic health decline. Due to dose-limiting toxicity, maximum cancer cell death is unachievable. Thus, we propose a ketogenic diet combined with fasting as an adjuvant therapy for chemoprotection in cancer patients. Carbohydrate restriction induces cellular repair pathways by inhibiting the insulin/IGF-1/mTOR pathway. Therefore, we hypothesise that metabolic ketosis will provide chemo-protection to healthy cells, while not benefiting cancer cells due to their constitutive activation of mTOR.

Aim: To test whether a ketogenic diet combined with fasting provides chemoprotection to healthy cells by activating DNA damage response and avoiding cell senescence in acute myeloid leukemia(AML) patients.

Methods: DNA repair and cellular senescence in response to chemotherapy was analysed using flow cytometry in healthy and cancer cells from AML patients. To confirm that the nutritional intervention does not favor cancer proliferation, the presence of Ki-67 in myeloid blasts was measured.

Results: Preliminary results from in vitro assays confirmed that chemotherapy induces DNA damage response and cellular senescence in healthy and cancer cells. Diagnostic bone marrow taken pre-intervention in AML patients showed high expression of Ki-67 in cancer blasts and low expression of DNA damage and cellular senescence markers. Additionally, the percentage of cancer cells pre-chemotherapy and diet is highly abundant, comprising 30-65% of total cells.

Conclusion: As expected, both healthy and cancer cells extracted from AML patients present low levels of DNA damage response before chemotherapy. However, the cancer cells are highly abundant and proliferative compared to healthy cells. Future experiments will test how the nutritional intervention affect these parameters pre- & post- chemotherapy.

Presenter Bio:
My research focuses on using the ketogenic diet/fasting as an adjuvant therapy for Acute myeloid leukemia patients and conducting molecular/cellular assays to measure proliferative, DNA damage and cellular senescence pathways. The clinical trial also involves direct clinical work with cancer patient as well as perfoming a diagnostic panel of Acute leukemia markers on the patients. This interdisciplinary project involves: Oncohaematology, Nutrition, Immunology, Molecular biology, Clinical research and Patient care.

13. Targeting Mitochondrial Metabolism and Tumour hypoxia as an approach to Improve the Radiation Response in Diffuse Midline Gliomas

Faiqa Mudassar* (1,2), Cecilia Chang (3), Prunella Ing (1,2), Kristina M Cook (2,4), Geraldine O'Neill (5,6), Han Shen# (1,2) and Eric Hau# (1,2,7,8)
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(7) Department of Radiation Oncology, Crown Princess Mary Cancer Centre, Westmead Hospital, Sydney.
(8) Blacktown Cancer and Haematology Centre, Blacktown Hospital, Sydney.

Background: Diffuse Midline Glioma (DMG) is uniformly fatal paediatric brainstem tumour with median survival of less than 1 year. Radiotherapy has been the only effective treatment for decades, but most DMGs recur within several months due to radioresistance. Hypoxia, a main feature of solid tumours including gliomas, is a major contributor to radioresistance as oxygenation is critical to successful radiotherapy treatment. Therefore, strategies to alleviate hypoxia could enhance the effectiveness of radiotherapy and result in improved survival outcomes of patients with DMG. Recent approaches to target tumour hypoxia are predicated on inhibiting mitochondrial respiration of the tumours to decrease oxygen consumption rate (OCR) and increase oxygenation.

Aim: Here, we aimed to identify potent mitochondrial inhibitors that could decrease OCR and hypoxia and improve the radiosensitivity of DMG.

Methods: We performed a high-throughput screening to identify potent OCR inhibitors using a library of 1963 FDA-approved drugs. Additional smaller OCR screening was also performed. Identified mitochondrial inhibitors were studied against a panel of patient-derived DMG cell lines. We assessed their anti-proliferative effects, OCR and hypoxia inhibition and radiosensitising efficacy using cell proliferation, extracellular flux assay, and colony formation assays.

Results: Two promising OCR inhibitors identified were atovaquone and mefloquine. Both the drugs reduced mitochondrial respiration, alleviated hypoxia, and decreased the expression of hypoxia-inducible factor-1a in 3-dimensional DMG neurospheres. Their anti-mitochondrial role was further confirmed by inhibition of various other mitochondrial parameters and increase in reactive oxygen species. These drugs have not been previously tested in combination with radiation on DMG cells and our study found, for the first time, that both the drugs also improved the radiosensitivity of DMG neurospheres.

Conclusion: Overall, these results provide promising in vitro evidence of atovaquone and mefloquine as hypoxia modifiers and radiosensitisers of DMG cells and pave a way for rapid translation to in vivo studies.

Presenter bio:
My research focuses on improving radiation response of the incurable paediatric brain tumour, Diffuse Midline Glioma (DMG), by targeting mitochondrial metabolism and tumour hypoxia. Currently, radiotherapy is the cornerstone of treatment for the management of these tumours, therefore, improving radiation response is a promising strategy to enhance the survival outcomes of patients with this deadly disease. Targeting mitochondrial metabolism and tumour hypoxia to improve radiotherapy is a novel area in DMG research. Additionally, our approach considers repurposing FDA-approved drugs for DMG treatment, hence providing a quicker approach for the translation of compounds from bench-side to the clinic.

Session 2a: Cell biology, molecular biology and biomarkers

14. Investigation of a novel therapeutic mechanism in aggressive leukaemia

Carla Jensen* (1,3), Jenny Wang (1, 2), Nunki Hassan (1,2)

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Acute myeloid leukaemia (AML) is an aggressive malignancy driven by leukemic stem cells (LSCs). Current therapeutics are ineffective at eradicating LSCs, which contribute to high relapse rates through its unlimited self-renewal capacity. Epigenetic therapy has the potential to be more effective against LSCs, due to its ability to correct aberrant gene expression. However, there are currently no effective therapies that directly target LSCs, partly due to a poor understanding of epigenetic mechanisms.

This study aimed to investigate the tumour suppressive activity of a newly identified epigenetic regulator in human AML and its regulation in LSC self-renewal.

Our preliminary data identified an epigenetic regulator that negatively regulates a key LSC self-renewal pathway. The epigenetic regulator was lentivirally introduced into a human AML cell line associated with poor prognosis. Cell proliferation was assessed followed by apoptosis and cell cycle analysis to determine the cause of altered proliferation rates. Its effect on self-renewal was evaluated by measuring the mRNA and protein expression of LSC self-renewal genes. Chromatin immunoprecipitation-quantitative PCR was performed to identify epigenetic changes on target genes. Statistical significance was determined using unpaired student's t-tests (n=3).

Our results showed that overexpression of the epigenetic regulator reduced AML cell proliferation by increasing the abundance of early apoptotic cells (p<0.05) but had no effect on cell cycle. It downregulated key self-renewal genes (p<0.001) and enriched the epigenetic regulator at a gene responsible for initiating LSC self-renewal capacity (p<0.01). The regulator could also remove an active epigenetic mark and lead to suppression of target genes.

Collectively, our study identified for the first time a new epigenetic regulator that acts as a tumour suppressor in aggressive AML by impairing self-renewal activity. This provides initial evidence supporting its tumour suppressive role for developing an effective AML therapy where the reversal of aberrant epigenetic marks could eradicate LSCs.

Presenter Bio:
Epigenetic therapy is a potential anti-cancer approach due to its reversible nature. My research is focused on investigating the tumour suppressive activity of an epigenetic regulator in aggressive AML. Additionally, we explored the regulatory role of the epigenetic regulator in LSC self-renewal to determine if the epigenetic regulator may serve as a therapeutic target to impair LSCs and hence eradicate this cancer-propagating cell population for therapeutic purpose.

15. The Tumour Microenvironment in Keratinocyte Cancers from Immunosuppressed Patients

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Keratinocyte cancers (KC) occur at significantly higher rates in organ transplant recipients (OTR). Nicotinamide is an effective chemo-preventative agent against KC in immunocompetent individuals. The role of Nicotinamide in immunosuppressed populations is not known. The ONTRANS study is a phase 3 randomised controlled study assessing efficacy of oral nicotinamide on KC incidence in OTRs, currently in data analysis phase. We have analysed the tumour microenvironment (TME) in invasive squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and SCC in situ (CIS) from organ transplant patients on study and evaluated the biologic effects of nicotinamide on it. We have used a novel, high-throughput technique called Imaging Mass Cytometry (IMC) which permits simultaneous analysis of 40 markers of interest at the single cell level.
Formalin fixed paraffin embedded (FFPE) tissues were used. Images were generated with the Hyperion imaging system (Fluidigm®). Immune phenotypes were identified with FlowJo™ and statistical analysis was performed on GraphPad Prism®. The final study population included tissue from 76 tumours.
There are significantly more B cells and Natural Killer (NK) cells in cSCC compared to BCC. There are significantly more B cells, NK cells and macrophages in tumours from liver transplant recipients compared to renal transplant recipients. CD4+ T cells, CD8+ T cells, proliferating T cells and T regulatory cells do not differ significantly between cancer types or tumours from different transplant types. Nicotinamide exposure does not affect the infiltration of major immune cell subsets. Fibroblasts comprise a major population of the TME, are differentially activated and express diverse markers.
The immune and stromal infiltrate is variable in KC from OTRs. Exposure to Nicotinamide does not affect the infiltrate of major immune cell populations. There are some differences in the TME between different KC types from OTRs. Fibroblasts are a major component of the TME with diverse phenotypes.

Presenter Bio:
My research focuses on the characterisation of the tumour microenvironment in Keratinocyte Cancers using a novel technology called Imaging Mass Cytometry. These are extremely common cancers, and rates in organ transplant recipients are up to 250 times that of the general population. Unfortunately, there are limited studies exploring the tumour microenvironment in tumours from this high-risk population. We hope to provide in depth analysis of hundreds of cell populations in these tumours and correlate our findings with clinicopathologic variables such as - tumour size, recurrence, peri-neural and lympho-vascular invasion, differentiation status and response to therapies. In future we hope to conduct a similar study in immunocompetent patients, and thereby understand how iatrogenic immunosuppression affects the tumour microenvironment.

16. Identifying and Matching Novel Combination Immunotherapies to the Correct Patients in Advanced Melanoma

Ella McCutcheon* (1,2,3), Richard A. Scolyer (1,2,3,4,5), Georgina V. Long (1,2,3,6,7), James S. Wilmott (1,2,3), Ines P. da Silva (1,2,3,8), and Tuba N. Gide (1,2,3)

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Background
While immunotherapy is currently the standard of treatment for unresectable melanoma, there are still large numbers of patients dying due to resistance. Novel immunotherapy combinations targeting anti-PD-1 with a GITR agonist or anti-LAG-3 therapy may benefit patients not responding to standard-of-care treatments. However, there is a lack of research on predictive markers of response to these novel immunotherapies.

Aims
This study aimed to identify the distinct immune profiles associated with response or resistance to anti-PD-1 plus GITR agonist or anti-LAG-3 combination immunotherapy.

Methodology
This study included 27 patients treated with anti-PD-1 + GITR agonist therapy (n=11 responders, n=16 non-responders), and 54 patients treated with anti-PD-1 + anti-LAG-3 therapy (n=37 responders; n=17 non-responders). Patients were categorised as responders (CR or PR) or non-responders (SD or PD) based on RECIST. Multi-plex immunofluorescence staining was performed on 81 pre-treatment (PRE), 20 early during treatment (EDT) and 16 post-progression formalin-fixed paraffin-embedded specimens to characterise the tumour immune microenvironment of responders versus non-responders. The panel included the markers CD3, CD8, PD-1, GITR/LAG-3, FOXP3, SOX10, and DAPI. Quantitative analysis was performed using HALO image analysis software.

Results
In the anti-LAG-3 therapy cohort, LAG-3 expression was observed on CD3+ T-cells in 95% of samples. While there was no significant difference in the level of CD3+LAG3+ T-cells between responders and non-responders, there was a trend towards higher levels of intratumoral CD3+ and CD3+PD1+ T-cells in responding patients (p=0.1567). Additionally, results showed an increase in CD3+CD8-LAG3+PD1+ cells from PRE to EDT in paired samples (n=6, p=0.063). GITR expression was observed on CD3+ T-cells 89% of samples in the anti-GITR patient cohort. No significant differences were observed in T-cell densities in this cohort (P>0.05).

Conclusion
Therefore, assessment of the tumour microenvironment via multiplex immunofluorescence may serve as a useful tool for guiding treatment decisions in patients with metastatic melanoma.

Presenter Bio:
While immunotherapy is currently the standard of treatment for unresectable melanoma, there are still large numbers of patients dying due to resistance. Novel immunotherapy combinations targeting anti-PD-1 with a GITR agonist or anti-LAG-3 therapy may benefit patients not responding to standard-of-care treatments. However, there is a lack of research on predictive markers of response to these novel immunotherapies. This study aimed to identify the distinct immune profiles associated with response or resistance to anti-PD-1 plus GITR agonist or anti-LAG-3 combination immunotherapy.

17. Biomarkers of Response and Resistance to Lenvatinib plus Anti-PD-1 in Advanced Melanoma

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Background
While there is a subset of advanced melanoma patients with long-term control of the disease with standard immunotherapy (anti-PD1+/-anti-CTLA-4), approximately half are resistant to the available treatments and die from melanoma. The novel drug combination, lenvatinib, (VEGF inhibitor) plus anti-PD-1, has shown promising results in patients resistant to standard immunotherapy. However, predictors of response to help guide treatment selection are yet to be identified.

Aims
This study sought to investigate the immune and transcriptomic profiles associated with response or resistance to combination lenvatinib plus anti-PD-1 therapy in patients with metastatic melanoma.

Methods
Thirty-seven patients with advanced melanoma treated with combination anti-PD-1 + lenvatinib therapy were included. Patients were classified as responders (CR or PR), or non-responders (SD or PD) based on RECIST. Multiplex immunofluorescence staining was performed on formalin-fixed paraffin-embedded specimens taken at pre-treatment (PRE; n=29), early during treatment (EDT; n=8), and at progression (PROG; n=9). The multiplex panel included the markers CD3, Granzyme B, CD31, CD14, PD-L1 and SOX10. RNA-sequencing will be used to compare the transcriptomic profiles of responders versus non-responders.

Results
Median age was 62 years and 65% were male. Seventy-one percent presented with stage M1C/D, 57% had elevated LDH, and 54% had previous anti-PD-1+/-anti-CTLA-4 treatment. The median proportion of intratumoural CD3+ T-cells was 6% for responders and 3% for non-responders. There was a trend towards an increase in peritumoural CD3+ T-cells from PRE to PROG (n=6; P=0.094). There was no significant difference in the proportion of intratumoural CD31+ cells between responders and non-responders (median= 2.8% in responders vs 3.1% in non-responders, P>0.05). Further analyses are underway, and will be presented at the conference.

Conclusions
The findings from this study will help to characterise and identify patients who will benefit from anti-PD-1 plus lenvatinib, meeting the large unmet need of patients resistant to available standard immunotherapies.

Presenter Bio:
The focus of my research is to look into a novel drug treatment for advanced melanoma and determine whether there are biomarkers of response or resistance to this novel treatment.

18. Investigating predictive biomarkers in adjuvant immunotherapy for stage III melanoma patients

Michael Xie* (1,2,3), Tuba N. Gide (1,2,3), Camelia Quek (1,2,3), Grace H. Attrill (1,2,3), Xinyu Bai (1,2,3), Georgina V. Long (1,2,3,4), Richard A. Scolyer (1,2,3,5) and James S. Wilmott (1,2,3)

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(5) Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital and NSW Health Pathology, Sydney, NSW, Australia.

Background
Melanoma is the leading cause of skin cancer-related deaths and is the third most commonly diagnosed cancer in Australia. Stage III melanoma patients have locoregional metastases without distant disease and have a prognosis that varies greatly with surgical resection alone. To decrease the risk of recurrence, adjuvant immune checkpoint inhibitor (ICI) therapy is administered following tumour resection. However, approximately half of patients will have tumour recurrence and some develop life-threatening drug-related side effects. Highlighting the need to identify biomarkers for patients who are more likely to benefit from adjuvant ICI treatment.

Aims
To investigate the genomic, transcriptomic and immune profiles of stage III melanoma patients who recur and do not recur within 1-year of commencing adjuvant immunotherapy.

Methods
This study included 118 patients with melanoma tissue samples collected before adjuvant anti-PD1 +/- anti-CTLA-4 immunotherapy. Patients who recurred within 1-year were defined as recurrence (n=50) and those who did not as recurrence-free (n=68). The median follow-up was 18.5 months. Targeted DNA-sequencing (486 gene panel) was performed for tumour mutational burden (TMB); high TMB was defined as more than 10 non-synonymous somatic mutations per megabase. Whole transcriptomic sequencing for differential gene expression analysis, and multiplex immunohistochemistry (mIHC) (CD68, CD16a, SOX10, PD-L1, CD8) for cellular composition.

Results
Recurrence-free patients had a significantly higher TMB compared to patients who developed recurrence (p=0.02). High TMB patients had longer progression-free survival compared to patients with low TMB (p=0.03). Transcriptomic profiles of recurrence-free patients demonstrated enriched signalling in pathways related to immune function, this is corroborated by preliminary mIHC findings of increased CD8+ T-cells and CD16+macrophages in the tumour microenvironment of recurrence-free patients compared to those who recur within 1 year.

Summary/Conclusion
Higher mutational burden and pre-existing inflammatory markers are associated with recurrence-free outcomes and may aid in deciding whether patients receive adjuvant immunotherapy.

Presenter Bio:
To investigate biomarkers for patients most likely to respond to adjuvant immune checkpoint inhibitor therapy to prevent unnecessary treatment-associated side effects.

Session 2b: Cancer treatments + Anti-cancer agents and drug development

19. Development of Novel Autophagy Inhibitors Based Anti-Cancer Combination Therapy

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Background: Autophagy is a cellular catabolic which is known to be activated by cellular stress and acts as a critical cell survival pathway. Solid tumours experience different microenvironmental metabolic stresses such as hypoxia and nutrient/energy deprivation. These highly stressful microenvironmental conditions could lead to activation of the pro-survival autophagic pathway, leading to cancer progression. Currently, clinically available autophagy inhibitors (e.g., chloroquine) only provides modest inhibitory activity. Hence, development of novel strategies to potently inhibit the autophagic pathway are warranted.

Methods: Triple negative breast cancer and oral cancer cell models were used for this study. Levels of autophagic marker, LC3-II, were determined by immunoblotting under different microenvironmental stressors. These results were further confirmed using immunofluorescence. We also utilized different autophagy inhibitors inhibiting two major regulatory complexes (ULK-1 and Beclin-1 complexes) in the core autophagic machinery. The synergy between different autophagy inhibitors and also, between autophagy inhibitors and standard chemotherapeutics (Paclitaxel and Cisplatin) was determined using Chou-Talalay method. Also, the most significant combination between the autophagic inhibitors and standard chemotherapeutics were tested in orthotopic mouse model for breast cancer.

Results: LC3-II was upregulated after incubation of cells under microenvironmental stressors in all cell models. Beclin-1 complex inhibitor (SAR405) and ULK-1 complex inhibitor (MRT68921) demonstrated significant ($p < 0.05$) inhibitory effect on cellular proliferation for all cell models used under different microenvironmental stressors. In the same context, cellular proliferation was significantly ($p < 0.05$) suppressed on combination of Beclin-1 complex inhibitor and standard chemotherapeutic (Paclitaxel or Cisplatin) in all cell lines under different microenvironmental stressors. In the orthotopic mice model, significant decrease in tumor size was observed in group of mice treated with combination of paclitaxel, Beclin-1 and ULK-1 complex inhibitors in comparison to control group ($p < 0.05$).

Conclusion: These studies demonstrate potential of utilizing autophagy inhibitors as a novel anti-cancer combination therapy.

Presenter Bio:
NA

20. Investigation of a novel drug candidate for human uveal melanoma

Sebastian Liau* (1), Janney Z. Wang (1), Nguyen H. Dang (1), Ethan Zagarella (1), Paus Paulus (1), Jingchun Gao (1), R. Max Conway (2,3), Li-Anne Lim (2,3), Svetlana Cherepanoff (4), Michael Murray (1), Fanfan Zhou (1)

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(2) Ocular Oncology Unit, Sydney Eye Hospital and The Kinghorn Cancer Centre, Sydney, NSW 2006, Australia
(3) Save Sight Institute, The University of Sydney, Sydney, NSW 2006, Australia
(4) SydPath, Department of Anatomical Pathology, St Vincent's Hospital, Darlinghurst, NSW 2010, Australia.

Background: Uveal melanoma (UM) is the primary ocular cancer with up to 50% of patients dying from metastatic disease. Although rare, it is deadly because patients with metastatic UM survive less than 18 months from diagnosis. To date, there have been no drugs with proven efficacy in UM. Furthermore, research endeavours in drug discovery and development have yielded unsatisfactory outcome in improving survival rates of UM patients. Thus, there is an urgent need to develop new drugs to treat UM. We have screened a panel of camptothecin derivatives, among which J11 showed the most potent effect in reducing cell viability across four immortalised UM cell lines.

Methods: The anti-cancer potency of J11 was evaluated in four immortalised UM cell lines with cell viability, ROS and cytotoxicity assay. The anti-metastatic potential of J11 was assessed with wound healing and clonogenic assay. The tumour selectivity of J11 was also investigated in non-tumour retinal cell lines and primary melanocytes.

Results: J11 treatment significantly reduced cell viability across all four UM cell lines (IC50 values ranged from 0.07 to 8.54 μM), which effect was accompanied with elevated ROS and increased cytotoxicity. J11 also potently inhibited cell migration and reduced reproductive cell growth in all tested cell lines. In addition, J11 showed mild to moderate cytotoxicity in non-tumour cells.

Conclusion: Our findings have indicated that J11 has potent anti-cancer and anti-metastatic effect against human UM. It may be developed as a novel and promising regimen in treating human primary and metastatic UM.

Presenter Bio:
I mainly focus on the effects of a novel compound J11 on uveal melanoma cell lines. I deploy a wide range of assays and methodologies to identify anti-cancer and anti-metastatic effect of J11.

21. Effects of [177Lu] Lu-PSMA-617 on overall survival in VISION versus TheraP randomized trials: An Exploratory Analysis

Yu Yang Soon* (1), Ian Marschner (1), Martin Stockler (1), Andrew Martin (1)

(1) NHMRC Clinical Trial Centre, University of Sydney

Introduction
Observed effects on overall survival differed in the first two randomized trials of Lu-PSMA in metastatic, castration-resistant prostate cancer. This study aimed to investigate the effects of crossover after progression on study treatment, and differences in comparator groups' treatments, as explanations for differences in the observed effects of LuPSMA on survival in these RCTs.

Methods
We performed the supplementary analysis of available individual participant data trial from TheraP (n=200) and VISION (n=831). TheraP randomized participants to treatment with either LuPSMA or Cabazitaxel (CBZ). VISION randomized participants to treatment with or without LuPSMA, in addition to physicians' choice among protocol-defined treatments, excluding CBZ. Rank-preserving structural failure time (RPSFT) and inverse probability of censoring weighting (IPCW) were used in TheraP to estimate treatment effects on OS had crossover not occurred in either treatment group or in both treatment groups. Individual participant data (IPD) on survival time from Vision extracted from published survival curves for comparison with IPD from TheraP.

Results
For the TheraP trial, 20 participants in CBZ group (n = 101) crossed over to LuPSMA while 32 participants in LuPSMA group (n = 99) crossed over to CBZ. There were no significant differences found from the TheraP trial in the OS between LuPSMA and CBZ had crossovers not occurred in either groups or both groups in TheraP (No crossover in CBZ: RPSFT HR 0.97, 95% CI 0.62 –1.52, IPCW HR 0.92, 95% CI 0.65-1.32; No crossover in LuPSMA: RPSFT HR 0.97, 95% CI 0.60–1.58, IPCW HR 0.82, 95% CI 0.55–1.24; No crossover in LuPSMA and CBZ: RPSFT HR 0.97, 95% CI 0.53-1.74, IPCW HR 0.82, 95% CI 0.53–1.27). Both LuPSMA treatment groups in VISION and TheraP RCTs have similar OS (HR: 0.92, 95% CI 0.70 - 1.19). The comparator treatment group in TheraP had longer OS compared to that of VISION (HR: 0.57, 95% CI 0.43 - 0.75)

Conclusion
The use of different comparators for control groups in these trials is a more compelling explanation than crossovers for the difference in LuPSMA's effect on OS in TheraP and VISION trials.

Presenter Bio:
Dr Soon graduated from the University of Sydney Medical School in 2009 and completed his residency training in Radiation Oncology at the National University Cancer Institute, Singapore in October 2016. He has also spent 6 months of his residency training at Peter MacCallum Cancer Centre in Australia. Dr Soon is a staff specialist in the Department of Radiation Oncology at at the National University Cancer Institute, Singapore since 2017. He has completed the Master of Science degree in Clinical Epidemiology at the Harvard University in May 2018. He is currently studying a PhD in clinical trial methodology at the NHMRC Clinical Trial Centre at the University of Sydney. He has a keen research interest in clinical trials and evidence synthesis.

22. CRISPR Based Knockout of HLA Class I and II to Prevent Allorejection of Off the Shelf Chimeric Antigen Receptor T-cells

Melanie Mach* (1,2), James Todd (1,2,4), David Bishop (3,4,5,6), Kavitha Gowrishankar (2,3,7), Kenneth Micklethwaite (1,2,3,4)

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(3) Westmead Clinical School
(4) Westmead Hospital
(5) St Vincent's Hospital
(6) Nepean Hospital
(7) Kids Research

Background: Chimeric Antigen Receptor T-cells (CART) targeting the B-cell antigen, CD19, have produced complete remissions in >90% of patients with chemotherapy-refractory Acute Lymphoblastic Leukemia and >50% in refractory Diffuse Large B-cell Lymphoma. However, CART are currently manufactured individually for each patient from autologous T-cells which is time-consuming and expensive. Furthermore, most CART therapies in the current clinical landscape use random gene-integrating techniques to insert the CAR transgene, with a potential risk of insertional mutagenesis. The availability of allogeneic, site-specific off the shelf CART from a healthy donor would markedly reduce the cost and enable their universal use. However, their efficacy may be limited by recipient T-cell mediated rejection of mismatched human leukocyte antigen (HLA).

Aim: We aim to generate off the shelf CART using CRISPR/Cas9 knockout of the T-cell receptor (TCR) complex. To mitigate CART rejection, we investigated knockout of various HLA Class I and II-associated gene targets, to directly disrupt HLA expression.

Methods: T-cell transfection by electroporation was performed with Cas9, single guide RNA and homology-directed repair template or PiggyBat transposon system on healthy peripheral blood mononuclear cell (PBMC), expanded for 3 weeks, and stimulated with interleukin-15 and irradiated autologous PBMC. Cell enumeration by trypan blue exclusion and multiparameter flow cytometry was performed at weekly intervals.

Results: CRISPR-edited CART exhibited comparable expansion, memory phenotypes and expression of immunoinhibitory molecules to transposon-edited CART produced with the nonspecific Super PiggyBac transposon system. In screening potential HLA-associated targets, we discovered a single novel target gene that efficiently downregulates HLA Class I and II expression on CART.

Conclusion: Our data demonstrates that CRISPR/Cas9 directed against novel targets can be used to efficiently generate CART lacking TCR and HLA. This developmental research will lay the crucial groundwork for the development of future off the shelf T-cell therapy products to target various malignancies.

Presenter Bio:
Melanie is a second-year PhD student producing 'Off the Shelf' chimeric antigen receptor T-cells (CART) which are genetically modified T-cells expressing an artificial receptor that enables them to target and lyse cancer cells. My project aims to utilise cutting-edge technologies and synthetic immunology, to generate novel, safe, anti-tumour CART in the laboratory that can be translated into effective therapy options.

23. A Computational Investigation to the Radiobiological Effects of Secondary Particles in Scanning Beam Proton Therapy

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(3) Northern Sydney Cancer Centre, Royal North Shore Hospital
(4) Ingham Institute for Applied Medical Research
(5) School of Biomedical Engineering, Faculty of Engineering, The University of Sydney

Objective: Proton therapy is an advanced radiotherapy modality which offers greater dose sparing potential to organs near the tumour. This study investigated the change in tumour control probability (TCP) and normal tissue control probabilities (NTCP) when alpha particle doses from proton nuclear interactions with tissue were incorporated into the calculations of the relative biological effect (RBE).

Approach: A 4-beam proton beam treatment plan was produced in EclipseTM and simulated in the TOPAS Monte Carlo toolkit. RBE-weighted dose maps were produced using 1) the current clinical RBE method, 2) an empirical proton RBE model and 3) an RBE method which incorporated proton and alpha particle doses.

Main Results: A clinically insignificant difference of 0.1 % was found between the TCPs for the three RBE methods tested. An NTCP increase was observed for the cervical spinal cord, brainstem, optic chiasm and right optic nerve when incorporating alpha particles to proton-only empirical models. The largest of these NTCP changes was 3.8% in the spinal cord.

Significance: This first investigation into the effects of alpha particles in a head and neck case indicates that alpha particle dose has a non-negligible impact on NTCP. This contrasts with the common assumption that the secondary hadrons are insignificant to proton therapy's radiobiological outcomes. This warrants further investigation into the effect of alpha particles with a patient cohort to assess their impact in different therapeutic scenarios.

Presenter Bio:
The focus of my research is the impact and potential utilisation of secondary hadrons produced in particle therapy through non-elastic nuclear interactions between the projectile particles and the nuclei of atoms in tissue. This research aims to investigate how the quantification and inclusion of secondary hadrons in relative biological effectiveness calculations could impact radiobiological predictions. Furthermore, this research aims to investigate how the production of secondary hadrons could be utilised to improve therapeutic outcomes in particle therapy.

Session 2c: Cell biology, molecular biology and biomarkers

24. Spatial characterisation of the tumour immune microenvironment in primary and metastatic melanoma

Grace H. Attrill* (1,2), Eva R. Shteinman (1,2), Xinyu Bai (1,2), Camelia Quek (1,2), Umaimainthan Palendira (1,2), Ismael A. Vergara(1,2), Georgina V. Long (1,2,3,4), Richard A. Scolyer (1,2,5,6), James S. Wilmott (1,2)

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(6) NSW Health Pathology, Sydney, NSW, Australia

Melanoma is one of the most highly immunogenic tumours, and the composition of the melanoma tumour immune microenvironment (TIME) has been associated with patient outcome in multiple tumour stages and treatment settings. In particular, increased B cell and CD39+ tumour-resident CD8+ T cell populations have been associated with reduced recurrence rates in primary melanoma and immunotherapy response in metastatic melanoma patients. However TIME composition can greatly differ between clinicopathologically identical patients, immune cell functions are highly dependent on their spatial contexture, and the spatial organisation of immune cells in the melanoma TIME is yet to be fully elucidated. Here, we aimed to utilise novel methods for cell spatial analysis that characterise the melanoma TIME, and to determine spatial proximity and neighbourhood associations with patient outcome in primary and metastatic melanoma. Two cohorts with available follow-up and clinicopathological data were studied: one of primary melanoma patients (n=46), and another of metastatic melanoma patients (n=119). Pre-treatment formalin-fixed paraffin-embedded tissue for both cohorts were stained using multiplex fluorescent immunohistochemistry to identify immune cell populations. Using the spatial analysis package SPIAT, immune-melanoma and immune-immune cell proximities were quantified using nearest neighbour, mixing and cross K analyses. Spatial cellular neighbourhoods were identified using the DBSCAN clustering algorithm. This revealed significant differences in the spatial contexture of the tumour, stroma and margins in the TIME based on outcome and tumour staging. Neighbourhood analysis also enabled identification and cellular composition assessment of lymphoid aggregates and candidate early tertiary lymphoid structures (TLSs). These cellular spatial relationships could provide further insights into immune cell function in the melanoma TIME and elucidate associations between TIME composition and patient outcomes.

Presenter Bio:
Grace is a final year PhD student studying tumour immunology at the University of Sydney and the Melanoma Institute Australia. She investigates the tumour immune microenvironment of melanoma in both the primary and metastatic settings, focusing on the anti-tumour CD8+ T cell response in melanoma patients. By performing highly multiplexed analyses of PBMCs and tumours from melanoma patients, Grace's work aims to identify and characterise tumour antigen-specific CD8+ T cells and ultimately improve immunotherapy outcomes for melanoma patients.

25. The role of metabolic stress in post-radiation tumour remodelling in human oral squamous carcinoma

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Background
The phenotypic switch along the epithelial-mesenchymal (E-M) axis of tumour cells is an important biological process demonstrated to positively associate with oncogenesis, tumour invasion, metastasis, and treatment resistance. Hyperglycaemia, or chronic exposure to high glucose levels, and its downstream factors are also involved in different mechanisms of tumour progression and therapy resistance in many types of cancer, including epithelial-to-mesenchymal transition (EMT).

Methods
In this study, we have established an in vitro model of hyperglycaemic stress and performed a range of cytological and transcriptome analyses to investigate the cellular and molecular roles of metabolic stress on tumour cell remodelling as part of the response to radiation of OSCC cell lines and the 3D OSCC tumour spheroids.

Results
The hyperglycaemic-stressed cells had an enhanced post-radiation survival rate, indicating resistance to ionising radiation. However, analysis of □-H2AX levels showed that there was no resolution taking place in the increased level of radiation-induced Double-stranded breaks (DBS) in the hyperglycaemic-stressed cells at 24hr post-radiation. An early increase in the number of epithelial-mesenchymal (E-M) hybrid cells, indicated by the presence of both phenotypic markers E-cadherin (ECAD) and Vimentin (VIM), at 2hr after radiation was observed in hyperglycaemic cells, followed by a significant elevation at the 24hr time point, highlighting enhanced plasticity through induction of an epithelial-mesenchymal hybrid phenotype. This observation was further confirmed through real-time RT-PCR analysis for the expression of EMT transcription factors.

Summary/Conclusion
Hyperglycaemic stress enhances resistance to radiation and the rate of radiation-induced EMT in OSCC tumour cells. In addition, the OSCC cells develop resistance to radiation not by resolving the genetic damage but via other pathways which involve the link between hyperglycaemic metabolic stress and tumour cell survival via EMT remodelling.

Presenter Bio:
NA

26. Establishment of an in-vitro Extra-cellular matrix model and its effect on therapeutic response

Maha Naeem Aman* (1), Grant Parnwell (2), Anna Guller (3), Ewa Goldys (3), Naisana S. Asli (1,4)

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Introduction: Tumor progression and its functionality is widely controlled by the local microenvironment immediately surrounding the cells of which the extra-cellular matrix (ECM) is a major player. During tumor homoeostasis and response to therapy, this non-cellular component is routinely destroyed and reconstructed to operate as a pro- or anti-tumorigenic medium [1, 2]. This study focuses on the role of ECM as a protective environment during the response of oral cancer cells (SCC 25) to treatment in order to better understand the function and processes underlying this shift in tissue architecture in a variety of situations.

Body: We have embarked on re-building a 3D cancer cell-ECM model by implanting carcinoma cells on to decellularized native murine tongue scaffolds to mimic true carcinoma and tested its response to radiotherapy in comparison to other study models that have been routinely used to analyze cancer progression.

Translation significance & Conclusion: This project will address the complex nature of tumorigenesis and tumor remodeling with regards to the cell-ECM interactome and will provide further insights into scaffold-mediated targeted therapy. Data from various imaging services and RNA-sequencing displays a clear trend favoring cancer growth in one of the models which will be universally beneficial to further examine they key characteristics of metastasis.

Presenter Bio:
The creation of innovative study models that can contribute in the treatment of cancer is central to Maha's research pursuits. She has a bachelor's degree in dental surgery and is thus particularly interested in researching oral cancer and its resistance to radiotherapy in order to be able to provide the impacted patients a better prognosis. She has a keen interest in clinical innovation research that promotes patients' quality of life in addition to her work on cancer.

27. Proteomic analysis of non-invasive biopsies of atopic dermatitis, psoriasis, and actinic keratosis for the identification of diagnostic biomarkers.

Lauren Faul* (1,2,3), Pablo Fernandez-Penas (1,2,3), and Ali Azimi (1,2,3)

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(2) Westmead Clinical School, Faculty of Medicine and Health, The University of Sydney
(3) Dermatology Department, Westmead Hospital

Background: Atopic dermatitis (AD), psoriasis, and actinic keratosis (AK) are common skin diseases that present as inflamed, red scaly patches. They often have overlapping clinical features, making their diagnosis often difficult.

Aim: To identify proteomic signatures that will allow for non-invasive and reliable diagnosis of atopic dermatitis, psoriasis, and actinic keratosis. As well as providing insights into their pathophysiology by investigating distinct molecular pathways and biological functions implicated in each lesion.

Methods: A total of 67 samples from patients with AD (n=20), psoriasis (n=10), AK (n=20) and normal skin (n=17) while attending a clinic at the Department of Dermatology, Westmead Hospital, were collected using adhesive discs. Following protein extraction from the discs, samples were analysed by mass spectrometry-based proteomics for protein identification and quantification. The resulting proteomic data was subjected to differential abundance analysis using linear modelling for microarray analysis (LIMMA) to identify protein signatures differentiating between the lesions. Classification and clustering analysis using a support vector machine (SVM) and principal component analysis (PCA) were performed on the data, followed by molecular pathway analysis using the Inequity Pathway Analysis (IPA) bioinformatics tool.

Results: Overall, 2202 protein groups were identified across all the samples studied, leading to the identification of IGHG4, IL36A, and PSMD14 proteins that could differentiate between AD, psoriasis, and AK respectively, from the normal skin samples (adj. p-value<0.05). PCA analysis identified most of the samples clustered according to their clinical diagnosis. In addition, SVM analysis correctly classified 76.5% of AD, 77.8% of psoriasis and 78.9% of AK according to their clinical diagnosis. IPA analysis of the proteomic data predicted important molecular pathways implicated in each lesion, opening unique opportunities for further research into their role in the development of the lesions.
Conclusion: Overall, this study has shown that proteomic analysis of non-invasive samples allows for the identification of lesion-specific biomarkers. Therefore, offering a unique opportunity for the development of a non-invasive diagnostic approach.

Presenter Bio:
Diagnosing skin lesions with the naked eye can be difficult, especially with lesions that have overlapping morphological features. Atopic dermatitis, psoriasis and actinic keratosis are just three common skin diseases that cause chronic inflammation and red scaly lesions. Due to these lesions having similar characteristics, patients may undergo painful biopsies and use unnecessary treatments due to misdiagnosis.

The use of a non-invasive scarless biopsy method called tape-stripping, and adhesive discs, can reduce the need for invasive diagnostic approaches. The adhesive disks collect skin cells, which contain proteins that can be extracted and analysed to identify lesion-specific biomarkers, using mass-spectrometry-based proteomics.

28. C-circle testing as an 'ALT'ernative Liquid Biopsy approach for Osteosarcoma

Ella Rose Dopper* (1), Lucy Cain (2), Vivek Bhadri (3), Anna Mullins (2), Geoff McCowage (2), Jeremy Henson (4), Melissa Griggs (1), Karen MacKenzie (5), Jonathan Karpelowsky (1), Smadar Kahana-Edwin (1)

(1) Advanced Molecular Diagnostics Group, Children's Cancer Research Unit, Kids Research, The Children's Hospital at Westmead
(2) The Cancer Centre for Children, The Children's Hospital at Westmead
(3) Chris O'Brien Lifehouse, Royal Prince Alfred Hospital
(4) University of New South Wales, Sydney
(5) Children's Medical Research Institute, Sydney

Background
C-circles are a marker of the Alternative Lengthening of Telomeres (ALT) mechanism which is present in approximately 59% of osteosarcomas. A method to identify C-circles in the plasma (P-ALT) could have the potential to diagnose ALT and monitor patients longitudinally.

Aims and Hypothesis
Our aim is to investigate the application of C-circle testing as a liquid biopsy approach for osteosarcoma. We hypothesise that as C-circles are a component of circulating tumour DNA (ctDNA), P-ALT will be proportional to disease burden.

Methods
DNA from tumours and plasma was subjected to the C-circle assay. The C-circle qPCR method was optimised by testing for optimal primer and input DNA concentrations accounting for the range of sensitivities of both plasma and tumour samples and used to classify samples as either ALT positive (ALT+) or negative (ALT-). Furthermore, C-circles levels were compared to clinically relevant indicators to deduce if they have any prognostic significance.

Results
Of 30 enrolled patients, ALT+ was detected in 12/21 (57%) available tumours. Of these 12 patients, 10 had plasma collected at diagnosis of which 8/10 (80%) were P-ALT+ and 6 patients had plasma collected at recurrence of which 5/6 (83%) were P-ALT+. Overall, 16 patients were classified P-ALT+ at diagnosis, 15 had a follow-up sample collected post 1 neoadjuvant chemotherapy cycle. A reduction of >50% C-circles between those time points corresponded to □95% necrosis in 7/9 (78%) of patients, while all 6 patients with increase or ≤20% reduction in C-circles had poor necrosis (range 20-40%) or disease progression.

Conclusion
We conclude that C-circles are found in the plasma as a part of the ctDNA and have the potential to be detected and quantified using a qPCR-based approach. Our results indicate that the identification of C-circles could assist in risk re-stratification after 1 cycle. C-circles in the context of measurable residual disease should be explored.

Presenter Bio:
The Advanced Molecular Diagnostics group in the Children's Cancer Research Unit focuses on identifying and monitoring cell-free circulating tumour DNA using Liquid Biopsy. This is a safe and minimally invasive technique that can be used to longitudinally monitor molecular changes, treatment response and possible disease recurrence.

Session 3a: Cell biology, molecular biology and biomarkers

29. Better Models for Better Breast Cancer Research: Could 3D models of non-invasive breast cancer reveal the key to invasive progression?

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Background: While mammographic screening has delivered improvements in breast cancer outcomes due to earlier-stage detection, its routine introduction has seen a ballooning of the detection of in situ lesions. Ductal Carcinoma in Situ (DCIS) is a non-obligate precursor of Invasive Ductal Carcinoma (IDC). Virtually all patients undergo surgery and adjuvant radiation, yet it is estimated that only 12% of untreated lesions would progress to IDC. However, current approaches have failed to elucidate a reliable biomarker that could spare a large majority of patients from unnecessary surgery and radiotherapy. The molecular signatures of DCIS and IDC are similar, suggesting the adjacent microenvironment, rather than tumour cells, may be regulating the invasive transition. Thus, there is a real need to use models that recapitulate the interaction of the tumour and microenvironment in modelling DCIS progression. Three-dimensional (3D) cultures have the potential to fill this gap in researchers' arsenal as a highly customisable platform that can reproduce different cellular and extracellular interactions.

Aim: To model the complex environment of DCIS using novel 3D approaches.

Methods: Three broad types of 3D culture have been employed: suspended spheroids, semi-embedded “overlay” cultures on matrix support, and matrix-embedded organoids. The latter are most flexible and can accommodate multi-layered approaches. We will compare the three approaches to assess the influence of key cell types within the microenvironment, on DCIS phenotype. This will be achieved using a variety of continuous cell lines and primary patient-derived organoids.

Results: Physiologically authentic co-culture of DCIS organoids with elements of the adjacent microenvironment will have the potential to reveal novel players in the transition to IDC, which will inform future clinical management of DCIS.

Conclusions: If successful, these novel biomarkers could provide reassurance in selecting patients at low risk of progression, to avoid surgery in favour of a program of regular imaging surveillance.

Presenter Bio:
It is rare to find someone whose life has not been touched by cancer, whether themselves or a loved one. During my undergraduate studies of immunology and applied medical science I became interested in the complexity and challenges of understanding and treating cancer. With the Translational Breast Cancer Genomic Group at Westmead Institute for Medical Research, I gained an understanding of the impact of DCIS that is only growing, and thus was excited to take on this project in cancer modelling that in future may assist both researcher and clinicians.

30. Cracking the genomic puzzle of paediatric cancer predisposition

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Background: Germline alterations in cancer predisposition genes (CPGs) are associated with increased risk of developing certain cancer types. Identification of childhood cancer patients carrying such genetic changes can assist in understanding why cancer develops in a child, improve patient care, and facilitate appropriate clinical management for the family. The ongoing PREDICT study conducted by our team aims to investigate germline alterations in newly diagnosed childhood cancer patients together with their parents (trio analysis) using whole genome sequencing (WGS).

Aim: My PhD project aims to establish bioinformatic pipelines to analyse germline trio WGS data against a panel of ~1000 cancer-related genes to identify (1) single nucleotide changes and small insertions/deletions, (2) canonical and non-canonical splicing variants, (3) copy number/structural variants, and (4) alterations in regulatory elements (e.g. promoter/enhancer), which may lead to cancer predisposition.

Methods: Trio-based WGS data are run through bioinformatic pipelines on the USyd High Performance Computing system. Variants are analysed using RStudio, incorporating online tools for curation, to prioritise novel variants.

Results: Using the established pipelines for Aims (1) and (2), 48 patients have been analysed thus far (35 patients with haematological malignancy, 13 with solid tumours). Pathogenic/likely pathogenic variants in clinically relevant CPGs (e.g. PMS2, NF1) were detected in 8/48 (16.7%) patients. In addition, 8 patients were identified to harbour novel candidate variants predicted to be functionally deleterious, and potentially associated with respective cancer types; including recurrent variants in DNA damage repair genes in patients with B-cell haematological malignancies. Further functional validation for selected variants-of-interest using relevant tumour samples and cell models are underway.

Summary: Comprehensive investigation of trio-based germline WGS, including but not limited to known clinically relevant CPGs, will greatly expand the capacity of detecting genomic alterations that may have been missed by conventional approaches. This may lead to discovery of novel mechanisms of cancer predisposition.

Presenter Bio:
I am a first year PhD student, conducting my research at the Children's Cancer Research Unit (CCRU) at Kids Research, The Children's Hospital at Westmead. My project is split into my two interests of bioinformatic analysis and experimental work. I analyse whole genome sequencing data from paediatric cancer patients using coding, combining various platforms and online tools, to identify any potential genetic variants of interest which may be increasing risk of childhood cancer. Additionally, I investigate the identified candidate variants of interest through experimental work, to understand the significance of those variants in the development of paediatric cancer.

31. Neurofilament Light Chain in Axonal Degeneration in Chemotherapy Induced Peripheral Neurotoxicity

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Background: Chemotherapy induced peripheral neurotoxicity (CIPN) is a common side effect of cancer treatment that typically manifests as sensory neuropathy. The mechanism of CIPN is not yet understood, however axonal degeneration is a common feature. Serum neurofilament light chain (NfL) is a potential protein biomarker of axonal degeneration but its role in predicting axonal damage in CIPN remains unclear.

Aim: To identify longitudinal changes in NfL in association with CIPN development in patients receiving the neurotoxic chemotherapy paclitaxel.

Method: CIPN was assessed using a clinical grading scale (National Cancer Institute -Common Terminology for Adverse Effects (CTCAE) neuropathy scale), neurological grading scale (Total Neuropathy Score clinical version) and patient reported outcome measures (EORTC- CIPN20; PRO-CTCAE) at three timepoints – beginning, middle and end of paclitaxel treatment. Serum samples were collected at the same timepoints and serum NfL was quantified using Quanterix SIMOA immunoassay.

Results: A total of 67 paclitaxel-treated patients (98% female, mean age 56±1.6 years) were recruited. Neuropathy incidence and severity increased over the course of treatment (p<.001). By end of treatment, 88% (n=59) had developed CIPN, which was mild in 55% (n=37, grade 1) and moderate/severe in 32% (n=22, grade 2/3). NfL mean concentration was significantly increased from beginning of treatment (45.2±16.1 pg/mL) to mid-treatment (151±18.5 pg/mL, p<0.001) and to end of treatment (191±16.0 pg/mL, p<0.001).

Conclusion: Serum NfL levels increased during paclitaxel treatment, in line with increasing CIPN severity. Quantification of serum NfL may provide a clinically useful marker of emerging neurotoxicity in patients who are vulnerable to CIPN.

Presenter Bio:
Identifying longitudinal changes in NfL in association with CIPN development in patients receiving the neurotoxic chemotherapy paclitaxel.

32. Detection and analysis of wrongly identified nucleotide sequence reagents in high impact factor cancer research journals

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(2) New South Wales Health Statewide Biobank, New South Wales Health Pathology, Camperdown, NSW

Background: With exponentially increasing numbers of research publications, studies that inform the reliability of published research are important to maintain high standards of research integrity and trust in science. Nucleotide sequence reagents can support biomedical research reliability, as they are widely used in genetics assays and their identities can be reliably fact-checked. Nucleotide sequences have also been extensively used to study the involvement of genes in human cancer. Previous studies have fact-checked nucleotide sequence reagents published in cancer and genetics journals with impact factors of 2-3, where unreliable research findings could be viewed to have limited influence on future research.

Aim: To identify whether problematic original articles describing wrongly identified nucleotide sequence reagents are published in high impact factor cancer research journals (impact factors>7).

Methods: We fact-checked nucleotide sequences in all original articles published in Molecular Cancer in 2014, 2016, 2018 and 2020 using Blastn and/or BLAT search algorithms against human and/or unrestricted nucleotide sequence databases. Using keywords identified in problematic Molecular Cancer articles in 2020, we also fact-checked selected Oncogene articles published in 2020.

Results: Of the 6,639 and 1,1388 nucleotide sequence reagents in original articles in Molecular Cancer and Oncogene respectively, 4.4% (295/6,639) and 4.8% (55/1,138) were wrongly identified. In total, 22% (110/500) original Molecular Cancer articles across the selected years and 39% (20/51) selected Oncogene articles in 2020 contained one or more wrongly identified reagents. Most problematic articles (Molecular Cancer, 59%, n=65/110; Oncogene, 55%, n=11/20) were authored by teams that were predominantly from China and affiliated with hospitals.

Conclusion: This study shows that original papers with wrongly identified nucleotide sequence reagents are unexpectedly frequent in high impact factor cancer research journals, where these papers could pose a serious problem for future research by the propagation of irreproducible findings or the reuse of wrongly identified reagents.

Presenter Bio:
Cancer research published in journals of high impact factor are cited a lot, well-exposed and often a career goal for many researchers. These papers are expected to be complex, compelling and foundational to our understanding of cancer as a disease. However, increasingly we have found problematic papers that describe wrongly identified reagents, which do not explain the published result in journals of all impact factors. The focus of this PhD project is to uncover problematic papers published in the higher echelons of journals i.e. journals of high impact factor that present the top 5% of journals publishing cancer research by impact factor, and identify their origins and significance to the greater, biomedical and cancer literature.

33. Machine learning-based proteomic prediction of squamous cell carcinoma subtype from 80 cancer cell lines

Emma L. Boys* (1), Zhaoxiang Cai (1), Karen MacKenzie (1), Jia Liu (1,2,3), Natasha Lucas (1), Daniel Bucio-Noble (1), Jennifer Koh (1), Erin Sykes (1), Steven G. Williams (1), Dylan Xavier (1), Peter G. Hains (1), Phillip J. Robinson (1), Qing Zhong (1), Roger R. Reddel (1)

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Background: Squamous cell carcinoma (SCC) is identified by immunohistochemistry staining for p63 and cytokeratin 5/6 but this cannot delineate SCC tissue site of origin. Further, SCCs from different tissue sites have overlapping risk factors. Diagnostic uncertainty can therefore arise in the setting of metastatic SCCs, which is important to resolve to select the most appropriate treatment.

Aim: To develop a machine learning (ML) classifier to determine site of origin in SCC cell lines using proteomic data obtained from data-independent acquisition mass spectrometry (DIA-MS).

Methods: DIA-MS data were obtained from 80 SCC cell lines (n=10 cervix, n=38 head and neck, n=13 lung, n=19 oesophagus). Proteomic data were processed using DIA-NN software. Supervised ML was used to train and test multinomial logistic regression models. Models were trained (80%) and tested (20%) using standardised protein intensity data. Optimal feature subsets were selected via recursive feature elimination with 8-fold cross validation. Evaluation metrics included accuracy, precision, recall, F1-score, and area under the receiver operator curve (AUROC). Pathway analysis was conducted using Reactome.

Results: Of 6692 quantified proteins, 55 proteins were included in the model with cervix, head and neck and lung SCC cell lines. Test accuracy was 85%; AUROC was 0.96. Pathway analysis revealed proteins involved in the cell cycle, mRNA regulation and glycolysis consistent with biology of the cell line entities. For example, cyclin dependent kinase inhibitor 2A, galectin-related protein and integrin beta-6 had utility in classifying cervical, lung and head and neck cancer cell lines respectively. When oesophageal cell lines were added to the model, test accuracy decreased to 50%; AUROC was 0.64.

Conclusion: Supervised ML using DIA-MS proteomic data can distinguish between some subtypes of SCC cell lines with high accuracy and AUROC. This approach may enable classification of SCC tumour subtypes, including SCC of unknown primary in future work.

Presenter Bio:
My research focuses on translating novel proteomic technologies, such as data-independent mass spectrometry and selected reaction monitoring, into the cancer clinic. This will be achieved by focusing on using proteomics to resolve several diagnostic dilemmas currently encountered in clinical practice including squamous cell carcinoma of unknown primary.

Session 3b: Clinical research

34. Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma: Clinical Outcomes by Genotype

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Background/Aim:
Diffuse Sclerosing Variant Papillary Thyroid Carcinoma (DSV-PTC) is associated with high rates of lymphatic and distant metastasis. DSV-PTC is associated with RET-fusions; however, the genotype-phenotype relationship is not established. We sought to characterise the driver mutations and their relationship with clinical outcome.

Methods:
DSV-PTC were identified from a pathology database and screened by BRAF V600E Immunohistochemistry (IHC). Wild-type BRAF samples were sent for targeted fusion and genomic sequencing. Outcomes were obtained from a prospectively maintained endocrine surgery database.

Results:
Over 20-years, 47 DSV-PTC samples were identified, eleven patients were excluded due to no tissue available for review or transformation to anaplastic carcinoma. The study population of 36 patients had a median age of 35 years, with 73% female and 81% of cancers had extra thyroidal extension, 89% lympho-vascular invasion and median 15 metastatic lymph nodes. BRAF V600E (IHC) was positive in 8 (22%) and genomic analysis of the remaining samples showed fusions including CDCC6-RET and novel ALK and NTRK. Both groups had similar presentation however BRAF wild type patients had higher rates of distant metastasis (14% vs 0%). Over a median follow-up of 4 years both groups received similar doses of radioactive iodine (6.6 GBq mean) and had similar rates of structural recurrence (43%). One (3%) BRAF wild type patients died from thyroid cancer.

Conclusions:
DSV-PTC has more genomic driver diversity than previously described, including fusions with ALK and NTRK. DSV-PTC demonstrates low level mortality but significant morbidity in the form of recurrence and reoperation. Fusion testing should be considered to guide management.

Presenter Bio:
Our research has focused on the diffuse sclerosing variant of papillary thyroid carcinoma. This variant disproportionately affects young women.
The exact prognosis of this variant is unknown as against the classic papillary thyroid carcinoma. In defining the prognosis and driver mutations of this variant we hope to encourage new treatment avenues for patients with complicated disease.
With time our hope is that particular driver mutations of disease are recognized as more aggressive than others. We hope that these variants may be treated with a more targeted approach using immunotherapies which could be superior to current treatment strategies.

35. Frequency and Characteristics of Errors performed by Artificial Intelligence in Reading Screening Mammography: A Systematic Review

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(4) Sydney Health Literacy Lab, Sydney School of Public Health, Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia

Background:
Artificial intelligence (AI) has comparable diagnostic accuracy in breast cancer detection in mammographic examinations, with possibility of tackling challenges of current human readers such as workload.
Previous studies have reported on the diagnostic accuracy of AI. However, characteristics of errors have not been thoroughly described. This systematic review aims to synthesise existing studies to identify types of AI errors, determine frequency of each type of errors, and describe its associated characteristics.

Methods
Studies that reported error made by AI and used externally-validated AI algorithms on real world mammographic screening examinations were included. Studies were identified via databases searches from January 2010 to June 2022 and reference lists. Two authors assessed the eligibility of studies with disagreements resolved via discussion. Two authors extracted data with (consensus procedure). Risk of bias in individual studies will be assessed using the QUADAS-2 tool. Data synthesis will be performed at study level on study and AI error characteristics, and diagnostic outcomes.

Results
Of the 1748 titles identified , 73 full text articles were reviewed. Nine studies totaling more than 694828 screened women met inclusion criteria. All studies were retrospective cohort studies with year range (2019-2022). Four studies were conducted in Sweden. Five studies reported AI used for triage. Four studies reported AI used as a standalone reader. Five studies reported on false negatives, 3 studies reported false positives, and 2 studies reported performance or technical error. Data extraction is currently underway and Risk-of-Bias Assessment will be performed after. Further findings will be presented.

Conclusion
This is the first systematic review to quantify and describe the extent of AI error reported in published literature. Following data syntheses, findings will inform whether and how AI and human errors might be different or similar. This is relevant for deciding how AI might supplement human screen-readings or diagnostic tasks.

Presenter Bio:
Aileen is a practitioner and also coordinator of the MRFF-funded Breast Tomosynthesis Research Program which aims to generate evidence on the accuracy of digital breast tomosynthesis (DBT) in some high-risk women (e.g. those with family history) or those with symptoms of breast cancer. Aileen's PhD investigates artificial intelligence (AI) errors to inform its application in breast cancer screening.

36. Methods for dealing with missing outcome data in randomised controlled trials: a methodological scoping review

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Background: Missing outcome data is a common occurrence when conducting randomised controlled trials (RCTs), including in cancer-related trials. While methods such as multiple imputation (MI) are increasingly used to handle missing data, complete case analysis remains a frequently used approach, despite its potential to underrepresent populations of interest, underutilise trial data and compromise trial validity.

Aim: Motivated by missing data issues encountered in a melanoma surveillance pilot trial (MEL-SELF) and the need to identify suitable methods to address these issues in the ongoing full MEL-SELF trial , we aim to conduct a methodological scoping review to identify and summarise methods for handling missing outcome data in RCTs.

Methods: We searched MEDLINE, EMBASE, CENTRAL, and CINAHL for articles in which authors discussed methods for handling missing data in RCTs. Two reviewers will undertake full text assessment and extracted data will be synthesised.

Results: 1842 unique articles were retrieved from the database searches. After full-text screening, 96 studies were included for data extraction. Preliminary findings indicate that MI is frequently discussed, with articles exploring the use of different types of MI under varied missing data assumptions (e.g., missing not at random) or missing data patterns (e.g., intermittent missing data or dropout). There are also new emerging methods incorporating machine learning techniques such as random forest (RF) imputation (including RF approaches using a causal inference perspective) and k-nearest neighbour techniques. Data extraction is currently underway, and results will be presented at the symposium.

Conclusions: This scoping review will synthesise evidence on different statistical approaches for handling missing outcome data in RCTs, and circumstances where one method may be preferred over another. Use of such methods in cancer-related trials may ensure better use of trial data so that there is fair representation of all trial participants, including those where data collection is incomplete.

Presenter Bio:
My research is focused on investigating new epidemiological methods to assist with the analysis of a randomised controlled trial of patient-led surveillance vs clinician-led surveillance for detection of subsequent new melanoma (the MEL-SELF randomised controlled trial). In particular, this research involves exploring missing data, causal inference and causal mediation methods.

37. Serum Metallome of Pancreatic Ductal Adenocarcinoma

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Pancreatic ductal adenocarcinoma (PDAC) is known for a high mortality rate that almost parallels the incidence rate. PDAC patients have a late diagnosis and poor prognosis due to asymptomatic characteristics of the disease until it has progressed to an advanced stage. Given that metal dyshomeostasis is known to play a role in cancer progression, this study aimed to determine the levels of 10 essential (magnesium, potassium, calcium, manganese, iron, copper, zinc, cobalt, molybdenum and selenium) and 3 toxic (arsenic, mercury and lead) metals in the serum of PDAC patients compared to age- and sex-matched healthy controls. Serum samples were obtained from PDAC patients who underwent surgical resection between 2004 and 2018, and samples were collected before their surgery. Inductively Coupled Plasma-Mass Spectrometry (ICP-MS) analysis was performed to quantify the level of metals in serum samples and statistical analyses showed dysregulated metals in PDAC and their role as a potential diagnostic and prognostic biomarker. A significant decrease was seen in the levels of magnesium, potassium, calcium, iron, zinc, selenium, arsenic and mercury, from PDAC patients compared to healthy controls. Selenium, iron, magnesium and calcium concentrations showed an area under receiver operator characterstic (AUROC) curve greater than 0.7, which indicated diagnostic potential of these metal concentrations in serum samples. Moreover, a significant decrease was identified in the overall survival of PDAC patients with lower levels of calcium, iron and selenium or higher levels of manganese. Since the blood metallome of PDAC patients has not been assessed yet, this is the first study to comprehensively assess serum metallome of PDAC patients that identified potential diagnostic and prognostic markers.

Presenter Bio:
My research focus involves metallomics and the tumour microbiome of pancreatic cancer, specifically looking at pancreatic cancer patients who were treated with neoadjuvant chemotherapy before they underwent surgical resection to determine the intra-tumoural microbiome and metallome of these patients.

Session 3c: Public health and psychosocial research

38. A review of mental health services in the diagnostic journey of cancer patients

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(1) Brain and Mind Centre, The University of Sydney

Mental health is an essential player in the diagnostic journey of cancer patients. This paper reviews the available literature on mental health in the diagnostic journey of cancer patients. The aim is to identify what available mental health support services cancer patients and their families have access to, what barriers exist in accessing these services, and what additional support is required. Addressing these questions will help identify the gap in delivering quality care to cancer patients and their families.

Presenter Bio:
There have been significant improvements in delivering mental health services to the public, and technology has played a crucial role. However, some gaps need to be addressed, particularly the delivery of mental health services to cancer patients and their families. A brief list of the unanswered questions include, are the mental health support services accessible to all cancer patients and their families, or are there conditions and requirements? Do socio-demographic factors influence access to these mental health support services? Addressing these questions can help improve mental health support services being delivered to cancer patients and their families.

39. Factors associated with psychosocial impacts of lung cancer screening: a systematic review

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Background
While lung cancer screening (LCS) can significantly decrease cancer-related mortality, there are a myriad of associated psychological impacts. Data from recent LCS trials suggests that psychosocial experiences are likely predicted or moderated by other factors (e.g., smoking status, experience with cancer and trait psychological factors), but the evidence has not yet been synthesised or critically appraised.

Aim
This systematic review investigated which factors impact psychosocial experiences of LCS.

Methods
Medline, Embase, PsycINFO and CINAHL were searched from inception to June 2022. Studies were included if they reported any predictor, moderator, mediator, or co-variate of a psychological or social outcome. Only LCS via low-dose computed tomography was considered, as this represents the current practice for LCS programs. Participants along the full continuum of LCS were included (i.e., from invitation/recruitment), but any studies which reported prospectively on potential or anticipated impacts of LCS were excluded. Given the heterogeneity in study design and outcomes, meta-analysis was not considered appropriate, and results were synthesised narratively. Quality assessment was undertaken using validated critical appraisal tools from the Joanna Briggs Institute according to study design.

Results
7,087 studies were identified from databases, with 5,520 studies remaining after removing duplicates. 87 full-text articles were screened following title and abstract screening, and 47 were chosen for inclusion. Of these, 31 studies reported on individual risk factors (e.g., sociodemographic characteristics, smoking status), 12 reported on modifiable service-level factors (e.g., communication of results, shared-decision making tools) and 4 reported on both. Included studies were conducted from 2001-2022.

Summary/Conclusion
Results are currently being synthesised. Findings will be presented for both individual and program-level factors which shape psychosocial experiences of LCS. These results will help inform a) who is at risk of psychosocial harm from LCS, and b) how to design LCS programs or targeted interventions to support them.

Presenter Bio:
My research centres around the psychosocial impacts of lung cancer screening, including test results, overdiagnosis and false-positives. With a national lung cancer screening program on the horizon, I am interested in developing strategies for improving associated psychological outcomes and supporting people through the screening process.

40. Prevalence of Epstein-Barr virus infection in China: a cross-sectional study

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Background
While almost every Chinese with nasopharyngeal carcinoma showed an Epstein-Barr virus (EBV) infection, the prevalence of EBV infection remains unknown.

Aim
We aimed to identify the prevalence of EBV infection in China and explore any risk factors.

Methods
This is a cross-sectional study conducted in a health management centre in Guangdong Province. Generally, healthy adults who underwent EBV viral capsid antigen (VCA IgA) test was included. Participants were further divided into groups based on their origin, endemic area (Guangdong, Guangxi, Hong Kong, and Macau) and non-endemic area.

Results
Between June 2021 and May 2022, a total of 8908 (4574 males and 4334 females) people were included in this study, of whom 6523 (73.2%) were from the endemic areas. An overall prevalence of 8.3% was obtained (95% CI 7.8 – 8.9). For the endemic areas, a prevalence of 8.8% (95% CI 8.1 – 9.4) was found, and that of non-endemic areas was 7.1% (95% CI 6.1 – 8.3; p = 0.01). Overall, prevalence was statistically higher in female (9.0%, 95% CI 8.1 – 9.8), male (7.7%, 95% CI 7.0 – 8.4; p = 0.03). No significant difference in sex was found within each group. Age was a risk factor (odd ratio 1.012, 95% CI 1.006 – 1.019). People aged 40 years old or above were more vulnerable to the infection, with a prevalence of 9.3% (95% CI 8.4 – 10.1), while for people under 40 years old, the prevalence was 7.3% (95% CI 6.5 – 8.1; p < 0.001).

Conclusion
Epstein-Barr virus infection is highly prevalent in the Chinese adult population, especially in southern China. The detection of EBV infection for people over 40 years old should be a public health priority in southern China to prevent and early identify NPC.

Presenter Bio:
NA

41. A systematic review of dentists' perceptions and practices towards dental care management in patients undergoing cancer therapies

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(2) Psycho-Oncology Co-operative Research Group (PoCoG)
(3) Sydney Dental Hospital and Oral Health Services

Background:
Cancer therapy can result in oral side effects such as mucositis, salivary dysfunction and myelosuppression. Systematic side effects such as nausea, vomiting and dysgeusia can result in poor diet and oral hygiene, putting the patients at risk of developing caries, periodontal disease and odontogenic infection. There is a lack of research in dental oncology and interest in managing dental health of patients undergoing cancer therapy for all malignant conditions.

Aims:
This systematic review aims to explore dentists' knowledge of knowledge of cancer, cancer therapies, their side effects and management of dental health and attitudes and experiences treating cancer patients.

Methods:
The systematic review is registered with Prospero. Database searches of Medline, Cinahl, Embase, Scopus and PsychInfo from the year 1990 based on key word and Mesh terms 'dentist', 'oral health' and 'cancer' were used to identify eligible articles. In addition, a hand search was performed from reference list of recent review articles and Google Scholar to capture additional articles. Articles were excluded if they are review articles, conference papers, expert opinions, non-English publication, paediatric population, or data for dentists could not be extracted.

Results:
The searches resulted in 2,103 articles after removing duplicates, and were uploaded onto Covidence. Two researchers independently screened the articles at title and abstract, and a total of 70 articles were included for full text review. A further 16 articles were excluded after reviewing full text, resulting in 54 articles for final data extraction. Currently, two researchers are independently extracting data from the full-text articles. Once both researchers have completed the data extraction, the data will be pooled and discussed. Preliminary observations found that most of the surveys are related to oral cancer knowledge and screening practices of dentists, while dentists involvement of other forms of cancer were minimally investigated. Most of the studies are quantitative self-reported surveys.

Presenter Bio:
I am interested in improving the dental health of cancer patients. I will be investigating the attitudes, beliefs, confidence, knowledge and experiences of dentists in treating cancer patients through a systematic review. I will also be investigating the barriers and facilitators of practicing dentists in Australia in treating cancer patients.

42. The impact of adopting the Anticancer Drug Dosing in Kidney Dysfunction guideline on Carboplatin dosing

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Background
Carboplatin dosing is calculated using the Calvert method to achieve a target AUC (area under the curve). A new international consensus guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD) recommends the use of BSA (body surface area) adjusted CKD-EPI in place of Cockcroft-Gault to estimate glomerular filtration rate (eGFR) , as it is considered more accurate .

Aim
To assess the impact of the new eGFR calculation on carboplatin dosing.

Method
A dosing simulation was created using two different calculations of eGFR, Cockcroft-Gault and the BSA adjusted CKD-EPI through the National Kidney Foundation eGFR Calculator . Variations in BSA, age, weight, serum creatinine and sex were analysed and generated a total of 21,600 dose simulations using a target AUC of 5. Clinically significant dose change was set at >10% difference.

Results
Discordance to Cockcroft-Gault calculation was at 57.37% for males (dose increase 42.85%; dose decrease 14.52%) and 80.65% for females (dose increase 33.87%; dose decrease 46.78%). Moderate renal impairment in younger populations required more dose reductions, while older populations with normal and mild renal impairment required more dose increases.

Discussion
Further studies and risk assessment on the impact of these dose changes on actual patients receiving carboplatin should be considered before implementation. A balance between dosing accuracy, efficacy and likelihood of adverse events should be considered.

Presenter Bio:
The gold standard for Carboplatin Dosing, has been based on the Calvert's Formula using the Cockcroft-Gault Equation. EVIQ has been open to using the CKD-EPI formula according to the Anticancer Drug Dosing in Kidney Dysfunction guideline.
On this basis we analyzed for statistical difference in therapeutic Carboplatin dosing, efficacy and potential side effects comparing a weight and BSA based formula, measuring Kidney function.

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