The Cancer Research Network Presents the:

2021 POSTGRADUATE & ECR CANCER RESEARCH SYMPOSIUM

9 December 2021

Virtual event

THE UNIVERSITY OF SYDNEY

2021 Postgraduate and ECR 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

We'd like to extend a warm welcome to the 13th Annual Postgraduate & ECR Cancer Research Symposium on behalf of the Postgraduate Student Working Group (PGSWG) of the University of Sydney Cancer Research Network.

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 pleased to announce that this year's symposium is in collaboration with Sydney Cancer Partners (SCP) and we invite you to tune in and hear about SCP's mission and goals from Professor Anna deFazio.

After another challenging year with COVID-19 impacting on our research and our lives, we were thrilled to have received so many abstract submissions, and we take the opportunity to thank all of you for sharing your research and supporting this year's symposium. As per tradition, the meeting will cover all aspects of cancer research, featuring work all the way from genomics and molecular biology to quality of life and survivorship. And to bring it all together, we could not have dreamt of a better keynote speaker: Dr Nicole Rankin – Convenor of AISN and Director of Implementation Science Program for Sydney Health Partners, who will be sharing highlights of her career as an implementation scientist and discussing how to optimise delivery of innovations in practice.

On behalf of the PGSWG, we would also like to extend our thanks to Marcel Batten, Susie Redfern and Cara McFarlane for their continued and unwavering support for this committee and this event. Huge thanks must also go to all the members of the PGSWG who have put in so much time and energy to organise this fabulous event.

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 #CRN2021Symposium and following us on @SydCancerNetwrk and @SydCancerPtnrs

Natalia Pinello, Nicola Fearn
Co-chairs, Postgraduate Student Working Group
Cancer Research Network

Keynote Speakers

Prof Anna DeFazio

BSc (Hons), PhD

Chair, the Cancer Research Network and Professor, Faculty of Medicine and Health, University of Sydney; Westmead Institute for Medical Research; Department of Gynaecological Oncology and The Crown Princess Mary Cancer Centre, Westmead Hospital; The Daffodil Center, a partnership between Cancer Council NSW and the University of Sydney;

Professor DeFazio holds the Sydney-West Chair in Translational Cancer Research, University of Sydney at Westmead Hospital, she Chairs the University of Sydney Cancer Research Network and she leads Sydney Cancer Partners. Professor DeFazio is the Director of the Center for Cancer Research, Westmead Institute for Medical Research and she leads the gynaecological cancer research program. Professor DeFazio's research is focused on understanding the clinico-genomic parameters that underlie treatment response and resistance in women with ovarian cancer, and she is the lead investigator on INOVATe, a program focused on molecular profiling, precision medicine and ovarian cancer clinical trials.

Dr Nicole Rankin

Senior Research Fellow (Implementation Science), Faculty of Medicine and Health, University of Sydney; Director, Implementation Science Program, Sydney Health Partners, University of Sydney

Dr Nicole Rankin is an implementation scientist whose research focuses on the science of research translation, including how evidence can be more rapidly translated into clinical practice, and how to improve patient and health service outcomes. Her expertise is applied across a portfolio of research projects, teaching and mentoring clinician-researchers in implementation science methodologies and leading communities of practice. In her role as Director of the Implementation Science (IS) Program at Sydney Health Partners (SHP), she is key to influencing the direction of the science and building capacity by leading the SHP Community of Practice (CoP). Dr Rankin's research background is in cancer control, focused on lung cancer and psycho-oncology. She has published more than 70 peer-reviewed manuscripts and has won $11.2M in research funding in the last five years. She has an active research portfolio that impacts directly on policy. Dr Rankin was awarded a Churchill Fellowship in 2020 and is a fellow of the Mentored Training in Dissemination and Implementation Research in Cancer program, Washington University in St Louis. She is an Associate Editor of Implementation Science Communications journal.

PROGRAM

2021 Postgraduate and ECR Cancer Research Symposium
Thursday 9th December 2021

Morning Zoom link: https://uni-sydney.zoom.us/j/89048603426		
OPENING AND WELCOME		
9:00	**WELCOME** Natalia Pinello and Nicola Fearn, PGSWG Chairs	
	OPENING ADDRESS by Prof Anna DeFazio, *Chair, the Cancer Research Network and Professor, Faculty of Medicine and Health, University of Sydney; Westmead Institute for Medical Research; Department of Gynaecological Oncology and The Crown Princess Mary Cancer Centre, Westmead Hospital; The Daffodil Center, a partnership between Cancer Council NSW and the University of Sydney*	
SESSION 1		
9:10	**Stream 1.1: Genomics and molecular biology (clinical)** Chair: Gemma Wilson, *The Westmead Institute for Medical Research*	**Stream 2.1: Quality of life** Chair: Chloe Lim, *Centre for Medical Psychology and Evidence-Based Decision Making, School of Psychology*
9:10	**Dr Braydon Meyer** **#001** Identification of DNA methylation biomarkers for prediction of response to neoadjuvant chemotherapy in triple-negative breast cancer *Garvan Institute of Medical Research*	**Ms Tiffany Li** **#026** Assessment of Chemotherapy-Induced Peripheral Neuropathy- A comparison of clinical, functional and patient reported approaches *School of Medical Sciences, Faculty of Medicine and Health, Brain and Mind Centre*
9:20	**Ms Arjayeeta Samadder** **#002** Overcoming Radio-Resistance by Reducing Tumour Oxygen Consumption in Diffuse Intrinsic Pontine Glioma *School of Medical Sciences, Faculty of Medicine and Health, Charles Perkins Centre*	**Dr Carolyn Mazariego-Jones** **#027** Priority Recommendations for the Implementation of Patient Reported Outcomes in Clinical Cancer Care: A Delphi study *Faculty of Medicine and Health, Daffodil Centre*
9:30	**Dr Geoffrey Yuet Mun Wong** **#003** Performance of prognostic models incorporating KRAS mutation status to predict survival after resection of colorectal liver metastases *Northern Clinical School, Faculty of Medicine and Health, Kolling Institute of Medical Research*	**Dr Vincent Singh Paramanandam** **#028** Prophylactic use of compression sleeves reduces the incidence of arm swelling in women at high-risk of breast cancer-related lymphoedema: a randomised controlled trial *Sydney School of Health Sciences, Faculty of Medicine and Health*
9:40	**Ms Tianyi (Eva) Gao** **#004** Cyclic and Stapled Peptides for Inhibiting the FANCM-RMI Interaction at Telomeres *School of Chemistry, Faculty of Science*	**Dr Chindhu Shunmuga Sundaram** **#029** Prevalence of concerns in Indian Head and Neck Cancer (HNC) populations reported on the Patient concerns Inventory (PCI): A brief report *School of Psychology, Faculty of Science, Centre for Medical Psychology & Evidenced-based Decision-making (CeMPED),Chris O'Brien Lifehouse, Quality of life Office*
9:50	**Dr Geoffrey Yuet Mun Wong** **#005** Recurrence patterns predict survival after resection of colorectal liver metastases *Northern Clinical School, Faculty of Medicine and Health, Kolling Institute of Medical Research*	**Ms Madeleine Juhrmann** **#030** Palliative Paramedicine: Comparing Clinical Practice through Guideline Quality Appraisal and Qualitative Content Analysis *Northern Clinical School, Faculty of Medicine and Health*
10:00	**SHORT BREAK (10 minutes)**	

SESSION 2		
10:10	**Stream 1.2: Genomics and molecular biology** Chair: Rachel Teh, *The Westmead Institute of Medical Research*	**Stream 2.2: Psycho-social** Chair: Nicola Fearn, *School of Health Sciences*
10:10	**Dr Pamela Soh** **#006** Profiling prostate cancer genetic risk associated with African ancestry *School of Medical Sciences, Faculty of Medicine and Health, Charles Perkins Centre, Garvan Institute of Medical Research*	**Ms Anna Singleton** **#031** Supporting breast cancer survivors via text messages: Reach, acceptability, and utility of EMPOWER-SMS *Faculty of Science, Engagement and Co-design Research Hub*
10:20	**Ms Safaa Al Haj Hussein** **#007** Decoding the genome of paediatric cancer patients to identify underlying germline genetic predisposition to cancer development *School of Medical Sciences, Faculty of Medicine and Health, Kids Research Institute (KRI)*	**Ms Kyra Webb** **#032** A systematic review and meta-synthesis examining fear of cancer recurrence in informal caregivers *School of Psychology, Faculty of Science, Psycho-Oncology Co-operative Research Group (PoCoG)*
10:30	**Ms Xinyu Bai** **#008** Identification of novel immunosuppressive mechanisms in adolescent and young adult (AYA) melanoma *Sydney Medical School, Faculty of Medicine and Health, Charles Perkins Centre, Melanoma Intitute Australia*	**Ms Ashleigh Sharman** **#033** Acceptability of an Evidence-Based Booklet for HPV-Related Oropharyngeal Squamous Cell Carcinoma Patients and their Partners *Sydney School of Public Health, Faculty of Medicine and Health*
10:40	**Ms Gaya Punnia-Moorthy** **#009** The role of KDM6A in melanoma *Central Clinical School, Faculty of Medicine and Health, Centenary Institute*	**Ms Chloe Lim** **#034** Psychosocial and quality of life experiences of people with advanced colorectal cancer: A mixed-methods study *School of Psychology, Faculty of Science, Centre for Medical Psychology & Evidenced-based Decision-making (CeMPED), Psycho-Oncology Co-operative Research Group (PoCoG)*
10:50	**Ms Gemma Wilson** **#010** Integrated Mapping of the Ductal Carcinoma In Situ Ecosystem to Predict Disease Outcome *School of Medical Sciences, Faculty of Medicine and Health, Westmead Institute for Medical Research*	**Ms Nicci Bartley** **#035** Stakeholder perspectives on the impact of COVID-19 on oncology services: A qualitative study. *School of Psychology, Faculty of Science, Psycho-Oncology Co-operative Research Group (PoCoG)*
11:00	**Ms Zoe Welham** **#011** The microbiome in bowel polyps *Northern Clinical School, Faculty of Medicine and Health, Kolling Institute of Medical Research*	**Ms Nicci Bartley** **#036** Experiences and perspectives of cancer patients/survivors, carers, cancer care healthcare professionals, and non-government cancer services, regarding COVID-19 vaccination *School of Psychology, Faculty of Science, Psycho-Oncology Co-operative Research Group (PoCoG)*
11:10	**LONG BREAK (2 hours 20 minutes)**	

Keynote Zoom link: https://uni-sydney.zoom.us/webinar/register/WN_U65Raa4US1CTIlA2y4E4Ng		
KEYNOTE SPEAKER		
1:30	**Dr Nicole Rankin,** *Convenor of AISN, Director of the Implementation Science (IS) Program at Sydney Health Partners (SHP); Senior Research Fellow, Implementation ScienceSydney School of Public Health* **Title: Implementation Science and Cancer Research: How do we optimise delivery of innovations in practice?**	
2:15	**SHORT BREAK (15 minutes)**	
Afternoon Zoom link: https://uni-sydney.zoom.us/j/83104519705		
SESSION 3		
2:30	**Stream 1.3: Cell biology and immuno-oncology (part 1)** Chair: Habib Francis, *Centenary Institute of Cancer Medicine and Cell Biology*	**Stream 2.3: Imaging, radiology and surgery** Chair: Andria Yaourtis, *School of Chemistry*
2:30	**Ms Maha Aman** **#012** ECM and its novelty in tumor progression *Faculty of Medicine and Health*	**Mr Sahand Hooshmand** **#037** A model to predict the lifetime dose and allocate a dose category from a single screening mammographic event *Faculty of Medicine and Health*
2:40	**Mr Mohammad Anisuzzman** **#013** Anti-Tumor Activity of Nimotuzumab and Trastuzumab Antibody Functionalized Gold Nanoparticles as a Potential Immunotherapeutic Agents Against Skin and Lung Cancers *Sydney Pharmacy School, Faculty of Medicine and Health, Bosch Institute*	**Mr Zeyad Alawaji** **#038** A systematic review reporting the computerised quality control of mammography phantom images *Sydney School of Health Sciences, Faculty of Medicine and Health,*
2:50	**Mr Daochen Tong** **#014** CD123-targeting Chimeric Antigen Receptor T-cells for treating Acute Myeloid Leukemia *Faculty of Medicine and Health, Westmead Institute for Medical Research*	**Ms Xuetong Tao** **#039** Varying Performance Levels for Diagnosing Mammographic Images Depending on Reader Nationality Have AI and Educational Implications. *Sydney School of Health Sciences, Faculty of Medicine and Health*
3:00	**Ms Vickie Chan** **#015** EGFR trafficking modes involved in cancer resistance to an immunotherapy. *Sydney Medical School, Faculty of Medicine and Health, Children's Medical Research Institute*	**Mr James Wood** **#040** An octadentate DFOB analogue to improve ligand performance in 89Zr-ImmunoPET imaging. *School of Medical Sciences, Faculty of Medicine and Health, Bosch Institute*
3:10	**SHORT BREAK (10 minutes)**	
SESSION 4		
3:20	**Stream 1.4: Cell biology and immuno-oncology (part 2)** Chair: Miguel Castaneda, *School of Medical Sciences and Charles Perkins Centre*	**Stream 2.4: Public health and cancer screening** Chair: Candice Donnelly, *Charles Perkins Centre*
3:20	**Ms Nancy Santiappillai** **#016** Fatty Acid Oxidation is a Minor Substrate Source to the TCA Cycle in Prostate Cancer Cells. *School of Medical Sciences, Faculty of Medicine and Health, Charles Perkins Centre*	**Mr Basel Qenam** **#042** Test-set training may increase breast screening cancer detection rates *Sydney School of Health Sciences, Faculty of Medicine and Health*

3:30	**Dr Robert Lu** **#017** Cell-cycle dependent regulation of non-productive and productive telomere synthesis in cancer cells engaging in Alternative Lengthening of Telomeres *Faculty of Medicine and Health, Children's Medical Research Institute*	**Dr Hankiz Dolan** **#043** Australian women's' intentions and psychological outcomes related to breast density notification and information: An online randomised experiment *Sydney School of Public Health, Faculty of Medicine and Health, Sydney Health Literacy Lab*
3:40	**Ms Natasha Freidman** **#018** Comfort eating: macropinocytosis as a resistance mechanism in breast cancer following glutamine transporter knockout. *School of Medical Sciences, Faculty of Medicine and Health*	**Ms Jenna Smith** **#044** General practitioner's attitudes and behaviours regarding cancer screening in older adults: A qualitative study *Sydney School of Public Health, Faculty of Medicine and Health, Sydney Health Literacy Lab*
3:50	**Ms Amy Sarker** **#019** PTU, a novel inhibitor of Wnt5a-mediated protrusions, inhibits High Grade Glioma cell invasion in 3-dimensional in vitro models *School of Medical Sciences, Faculty of Medicine and Health, Kids Research Institute (KRI)*	
4:00	**SHORT BREAK (10 minutes)**	
SESSION 5		
4:10	**Stream 1.5: Novel treatments** Chair: Josef Gillson, *Bill Walsh Laboratory, Kolling Institute, Northern Clinical School*	
4:10	**Dr Huaikai Shi** **#020** Leptospermum extras suppress malignant pleural mesothelioma tumour growth in vitro and in vivo *Asbestos Diseases Research Institute*	
4:20	**Ms Candice Maria Mckertish** **#021** Dual payload ADC approach to target and treat HER2+ breast and colon cancer cells. *Sydney Pharmacy School, Faculty of Medicine and Health*	
4:30	**Mr Reginald Young** **#022** Peptide-based inhibitors for targeting telomerase-active cancers *School of Chemistry, Faculty of Science*	
4:40	**Mrs Farhana Azmi** **#023** Developing renal clearable nanoparticles for the treatment of renal cell carcinoma *Westmead Clinical School, Faculty of Medicine and Health, Westmead Institute for Medical Research*	
4:50	**Ms Melanie Mach** **#024** Off the Shelf Chimeric Antigen Receptor T-cells for Malignancy: A nonviral and site-specific approach *Westmead Clinical School, Faculty of Medicine and Health, Westmead Institute for Medical Research*	
5:00	**Ms Farhana Mollah** **#025** A new strategy to overcome Triple-Negative Breast Cancer metastasis: combining novel targeted therapeutic candidates with an anti-Breast Cancer Associated Fibroblast agent *Sydney Pharmacy School, Faculty of Medicine and Health*	
5:10	**CLOSING MESSAGE AND END OF SYMPOSIUM**	
5:10	**END OF SYMPOSIUM**	

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ABSTRACTS

Stream 1.1: Genomics and molecular biology (clinical)

Ab#001 Identification of DNA methylation biomarkers for prediction of response to neoadjuvant chemotherapy in triple-negative breast cancer

Braydon Meyer* (1), Phuc-Loi Luu (1,2), Qian Du (1,2), Dilys Lam (1), Niantao Deng (2,3), Kate Harvey (3), Alex Swarbrick (2,3), Vinod Ganju (4), Susan J. Clark* (1,2), Ruth Pidsley* (1,2), Clare Stirzaker* (1,2) *equal

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(2) St. Vincent's Clinical School, UNSW Australia, Sydney, New South Wales, 2010, Australia
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(4) Hudson Institute of Medical Research, Clayton, Victoria, 3168, Australia

Background: Triple-negative breast cancer (TNBC) makes up 10-15% of all newly diagnosed breast cancers and is associated with a higher risk of disease recurrence and shorter overall survival compared to other subtypes. Neoadjuvant chemotherapy (NAC) is typically applied in the TNBC setting, and the degree of pathological response to NAC correlates with long-term prognosis. The response to NAC in TNBC is highly variable and poorly understood. Therefore, there is a pressing need to develop biomarkers to accurately predict NAC response allowing personalised chemotherapeutic decision-making approaches within the clinic and avoiding unnecessary toxicity from chemotherapy.

Aim: We aim to identify a DNA methylation-based biomarker panel to accurately predict response to NAC in TNBC patients.

Methods: We performed whole-genome DNA methylation profiling using the Illumina MethylationEPIC BeadChip microarray on 32 diagnostic TNBC patient biopsies from a neoadjuvant chemotherapy clinical trial, the Sequential Evaluation of Tumours Undergoing Preoperative (SETUP) study. Patients categorised as responders and non-responders were compared to discover differentially methylated regions (DMRs) associated with NAC response.

Results: We discovered nine significant differentially methylated regions (adj.P<0.1) in primary diagnostic TNBC biopsies that predict response to NAC. These 'response-DMRs' are hypermethylated in non-responders, are all localised within gene promoter regions and associated with cancer-related pathways. Using receiver operating characteristic (ROC) analysis we showed that we can also distinguish complete from partial response to NAC with high sensitivity of (AUC=0.891). Furthermore, we found that four of these DMRs are associated with TNBC overall survival (P<0.05).

Conclusions: Our results highlight the potential of DNA methylation biomarkers to be used as predictive biomarkers of response to NAC in TNBC. The utility of these biomarkers for predicting treatment response and long-term prognostic outcome does require validation, however this study creates a solid foundation for developing tailor-made biomarkers to specific NAC regimes.

Ab#002 Overcoming Radio-Resistance by Reducing Tumour Oxygen Consumption in Diffuse Intrinsic Pontine Glioma

Arjayeeta Samadder (1,3)*, Cecilia Chang (2,3), Faiqa Mudassar (2,3), Harriet Gee (2,3,4), Eric Hau (2,3,4), Han Shen (2,3) and Kristina M Cook (1,3)

(1) The University of Sydney, Charles Perkins Centre
(2) Translational Radiation Biology and Oncology Laboratory, Centre for Cancer Research, Westmead Institute for Medical Research
(3) The University of Sydney, Sydney Medical School, Faculty of Medicine and Health
(4) Sydney West Radiation Oncology Network

Background: Diffuse Intrinsic Pontine Glioma (DIPG) is a rare and fatal high grade pediatric brain tumour that typically affects children between 4 and 11 years old with a mean survival of ~1 year from diagnosis. Since DIPG tumours are located in the brainstem, making surgical removal impossible, radiotherapy is the only viable treatment. However, DIPGs typically recur within a year following treatment due to radio-resistance. DIPG tumours are characterised by poor blood and oxygen perfusion and a hypoxic tumour microenvironment. Since radiotherapy uses oxygen to be effective, hypoxia is a major cause of radio-resistance. Previous studies have established that biguanides like metformin and phenformin inhibit mitochondrial respiration in DIPG tumours, a major consumer of oxygen, thus, overcoming tumour hypoxia and radio-resistance in animal models of DIPG and other tumours.

Aim: Our aim was to identify more potent, repurposed drugs that inhibit mitochondrial respiration in DIPG cells and increase the efficacy of radiotherapy.

Methods: We screened a panel of 1963 FDA-approved drugs using the seahorse assay which measures tumour cell oxygen consumption rate (a marker of mitochondrial respiration) and extracellular acidification rate (a marker of anaerobic respiration or glycolysis), before and after drug injection. This enabled us to study the efficacy of drugs in reducing tumour oxygen consumption which may overcome tumour hypoxia and radio-resistance in DIPG.

Results and Conclusion: We have identified ~80 compounds that inhibit mitochondrial respiration in DIPG cells which will be further tested in combination with radiotherapy in in-vivo orthotopic pre-clinical models of DIPG with the aim of progressing into clinical trials in the future. Developing this treatment strategy to enhance radiotherapy efficacy may prolong survival in children with DIPG.

Ab#003 Performance of prognostic models incorporating KRAS mutation status to predict survival after resection of colorectal liver metastases

Geoffrey Yuet Mun Wong (1,2), Nazim Bhimani (1,2), Barend Mol (1,2), Connie Diakos (3), Philip de Reuver (4), Mark P Molloy (5), Thomas J Hugh (1,2)

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(2) Northern Clinical School, University of Sydney, Sydney, New South Wales, Australia.
(3) Department of Medical Oncology, Royal North Shore Hospital, Sydney, New South Wales, Australia.
(4) Department of Surgery, Radboud University Medical Centre, Nijmegen, Netherlands.
(5) Bowel Cancer and Biomarker Research Laboratory, School of Medical Sciences, University of Sydney, Sydney, New South Wales, Australia.

Background: This study aims to evaluate the performance of two novel prognostic models that incorporate KRAS mutation status to predict survival after resection of colorectal liver metastases (CRLM); Genetic and Morphologic Evaluation (GAME) score and modified clinical score (m-CS).

Methodology: A total of 103 patients who underwent resection of CRLM between 2007 and 2017 and had known KRAS mutation status were included, 39 (37.9%) of whom had KRAS mutant tumours. Complete case analysis of the patients was performed according to the Clinical Risk Score (CRS), m-CS, and GAME score. The primary outcome was overall survival stratified according to low-risk and high-risk scores. Harrell's C-index and Akaike information criterion (AIC) was used to compare the discrimination of the evaluated prognostic models.

Results: The GAME score demonstrated the most significant difference in overall survival for patients stratified into low-risk and high-risk groups. Harrell's C-index values for the CRS, m-CS and GAME models were 0.583, 0.600, and 0.668, respectively. AIC values for the CRS, m-CS and GAME models were 441, 439, and 427, respectively.

Conclusion: The GAME score outperforms the CRS and m-CS in predicting overall survival after resection of CRLM in patients with known KRAS mutation status.

Ab#004 Cyclic and Stapled Peptides for Inhibiting the FANCM-RMI Interaction at Telomeres

Tianyi (Eva) Gao*(1), Quynh Ngoc Vu (1), Haritha Krishna Sudhakar (1), Yu Heng Lau (1)

(1) School of Chemistry, The University of Sydney

Telomeres are repetitive sequences located at the end of chromosomes to prevent loss of genetic information due to the semi-conservative nature of DNA replication. As a result, telomeres shorten after each cell division until a critical length triggers the DNA damage response, leading to cellular senescence or apoptosis. About 5-15% of the cancer cells utilise an alternative lengthening of telomeres (ALT) mechanism to maintain telomere length and acquire immortality.

ALT activity is regulated by two protein complexes – FANCM and the Bloom's complex – which associate via a strong hydrophobic interaction between the MM2 domain of FANCM and the RMI subcomplex of the Bloom's complex. Removal of MM2 from FANCM completely abrogates the interaction with RMI, which is lethal to ALT-positive cells, providing a possible pathway to treatment for ALT cancers.

The aim of this project is to develop peptidomimetic inhibitors of FANCM-RMI interactions. In this presentation, I will discuss the design of cyclic analogues of the MM2 peptide, including the introduction of non-native amino acids and our progress toward stapling using different types of linkers. I will also discuss the use of cyclic peptide mRNA-display libraries to screen for inhibitors, and report the results of in vitro studies performed on resynthesised hits which have shown potent affinity (<30 nM) without needing further optimisation.

Ab#005 Recurrence patterns predict survival after resection of colorectal liver metastases

Geoffrey Yuet Mun Wong (1), Nazim Bhimani (1), Barend Mol (1), Connie Diakos (2), Philip de Reuver (3), Mark P Molloy (4), Thomas J Hugh (1)

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(2) Department of Medical Oncology, Royal North Shore Hospital, Sydney, New South Wales, Australia.
(3) Department of Surgery, Radboud University Medical Centre, Nijmegen, Netherlands.
(4) Bowel Cancer and Biomarker Research Laboratory, School of Medical Sciences, University of Sydney, Sydney, New South Wales, Australia.

Background: Effective treatment of colorectal liver metastases (CRLM) is challenging because recurrence occurs in many patients after curative-intent resection. This study evaluates the recurrence patterns after resection of CRLM and the association with survival.

Methodology: A retrospective review of prospectively collected data of patients with CRLM managed with curative-intent resection from January 2007 to December 2017 was performed. The main outcomes and measures were the timing of recurrence, initial sites of recurrence, overall survival and recurrence-free survival. Early recurrence was defined as the detection of any organ recurrence ≤6 months from resection of CRLM.

Results: A cohort of 194 patients managed with curative-intent liver resection for their first presentation of CRLM was included for analysis. After a median follow-up of 85.3 months, 145 patients (74.7%) were diagnosed with a recurrence. The median overall survival was 67.6 months (95% CI 50.4 – 80.2), and the 5-year overall survival was 54.1%. After initial recurrence was detected, the median survival was 28.9 months (95% CI 23.6 – 37.8) months, and the 5-year overall survival was 28.8%. Early recurrence occurred in 58 patients (29.9%). Initial recurrence patterns included: liver only in 53 patients (36.5%), multiple sites in 48 patients (33.1%), lung only in 30 patients (20.7%), and other single extrahepatic sites in 14 patients (9.6%). Early recurrence and initial multi-site recurrence were independent predictors of worse overall survival for patients who develop recurrence after resection of CLRM.

Conclusion: The timing and initial site of recurrence are prognostic factors in determining survival after curative-intent resection of CRLM.

Stream 1.2: Genomics and molecular biology

Ab#006 Profiling prostate cancer genetic risk associated with African ancestry

Pamela XY Soh* (1,2), Jue Jiang (2), Weerachai Jaratlerdsiri (1,2), Vanessa M Hayes (1,2)

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(2) Laboratory for Human Comparative & Prostate Cancer Genomics, Garvan Institute of Medical Research, Darlinghurst, Australia

Background: African ancestry is a significant risk factor for prostate cancer (PCa), suggesting a link to inheritance. Although a recent multi-ancestry meta-analysis identified 269 risk variants, with a bias towards African Americans, studies within the African continent are lacking.

Aim: Observing significant PCa mortality rates in Southern Africa, double those reported for the United States or Australia, we aimed to generate the first genome-wide association data for the region. Focusing on potentially functional exomic associations, we further assessed whole-genome sequenced (WGS) data for viability of known PCa risk variants.

Methods: Age-adjusted logistic regression analyses were conducted for 450 PCa cases and 293 controls of African ancestry, genotyped on the Illumina HumanExome-12 BeadChip v1.0, assaying 247,870 single nucleotide polymorphisms (SNPs). Deep whole-genome sequencing (WGS) data was available for an additional 110 population-matched cases, in which the allele frequencies for 269 previously identified PCa risk variants were calculated.

Results: While there was no significant genome-wide association found in the regression analyses, intriguing candidates were among the top 18 SNPs (P<0.0005). While three SNPs lay within HCP5, notable candidates included a SNP in RFX6, previously identified as a PCa risk in Asian men, and SNPs near the androgen-repressed gene NRP1 and the tumour suppressor CDH13. Of the 269 known risk SNPs in the 110 WGS cases, 46 (17%) were fixed for the reference allele and 39 (14%) had >0.1 difference in risk allele frequency compared to previously reported African controls.

Conclusions: While identifying SNPs within or near genes known to be involved in PCa, we are conscious of the limitation of sample size in our study and across Africa. Our study highlights significant needs required to unravel the aetiology of PCa ethnic disparity, firstly we call for the inclusion of Africa in global studies and secondly the need for whole-genome interrogation.

Ab#007 Decoding the genome of paediatric cancer patients to identify underlying germline genetic predisposition to cancer development

Safaa Al Haj Hussein* (1,2), Dianne Sylvester (2), Bhavna Padhye (3), Rebecca Harris (3), Sarah Josephi-Taylor (4), Geraldine O'Neill (2,5), Luciano Dalla Pozza (3), Yuyan Chen (2,5), PREDICT Study Team (6)

(1) Discipline of Applied Medical Science, Faculty of Medicine and Health, The University of Sydney
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(3) Cancer Centre for Children, The Children's Hospital at Westmead
(4) Clinical Genetics Department, The Children's Hospital at Westmead
(5) The Children's Hospital at Westmead Clinical School, Faculty of Medicine and Health, The University of Sydney
(6) Sydney Children's Hospitals Network and Children's Cancer Institute

Background: Cancer is a genetic disease resulting from an accumulation of somatic changes over time and is associated with ageing and environmental influences. However in paediatric patients, emerging evidence has shown germline alterations in cancer predisposition genes (CPGs) are associated with an increased risk of developing certain types of cancer. Advancing current understanding of CPGs in childhood cancer development is imperative for guiding therapeutic decision-making and disease surveillance, for both the patient and family members.

Aim: This study aimed to sequence germline DNA of paediatric cancer patients and parents (trio) and bioinformatically analyse single nucleotide variants, splicing variants and small insertions and deletions in known CPGs and cancer-related genes.

Methods: Blood samples were collected from paediatric cancer patients (n=15) and their parents enrolled in the Cancer Predisposltion in Childhood By Trio-Based Sequencing (PREDICT) study, with DNA extracted and subjected to whole genome sequencing. The ANNOVAR software was used to annotate variants which were filtered out to five curated gene lists (clinically actionable CPGs, other known CPGs, potential CPGs, DNA repair genes and other cancer-related genes). A rare variant analysis pipeline was followed to identify clinically reportable pathogenic/likely pathogenic (P/LP) variants and candidate research variants of interest.

Results: Two out of 15 patients were identified to have clinically relevant pathogenic variants in RET and ELP1 genes in concordance with cancer phenotype. Two patients carried likely pathogenic variants in MITF and ATR genes, however associations with respective cancer phenotypes are uncertain. Promising novel candidate variants were also identified, warranting further investigation.

Summary: The work carried out thus far has showcased the necessity and significance of analysing the germline genome to identify underlying genetic changes that may predispose paediatric patients to cancer development. The ongoing study will lead to more discoveries in known CPGs, as well as novel candidate CPGs for further functional validation.

Ab#008 Identification of novel immunosuppressive mechanisms in adolescent and young adult (AYA) melanoma

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There is a current lack of effective treatment for advanced stage AYA melanoma patients aged 15 to 30 years. Immunotherapies that target the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) or programmed cell death protein 1 (PD-1) pathways, which have drastically improved the 5-year overall survival of melanoma patients from 5% to 50%, are clinically shown to be less responsive in AYA patients. Better understanding of its unique genomic biology and clinicopathological patterns may explain the therapy-resistance of AYA melanoma, and help identify targets for combinatory treatment and/or patient stratification. The primary aim of this study was to determine the distinct patterns of treatment response and immunosuppression present in the melanoma biopsies of AYA patients. Whole transcriptome sequencing, bioinformatics analysis and multiplex immunofluorescence (mIF) were performed on formalin-fixed paraffin-embedded melanoma tumour samples taken at baseline from AYA patients (n=46) and adult patients (n=71) treated with anti-PD-1 and/or anti-CTLA-4 immunotherapy. Immune deconvolution demonstrated lower proportions of plasma cells, M2 macrophages and CD8 T cells (95%CI: 0–1.48% versus 2.32–5.80%; P-value = 0.0036) in AYA tumours compared to adult. mIF analysis demonstrated a trend of lower tumour infiltrating CD8:FOXP3 T cell ratio in AYA compared to adult melanomas (mean = 7.93 versus 19.9). AYA immunotherapy non-responders demonstrated higher regulatory T cell (Treg; CD4+FOXP3+) accumulation in intra- and peri-tumoral regions compared to AYA immunotherapy responders. Higher Treg density was correlated with lower intratumoral endothelial cell proportion and the downregulation of genes (ICAM3, VCAM1, CD6; adjusted P-value < 0.05) implicated in the cell adhesion pathway. By integrating our immune and genetic findings, we uncovered features of immunosuppression orchestrated by the tumour microenvironment in AYA melanoma, and derive a predictive signature for the poorly immunogenic tumour phenotype in AYA patients. Novel treatments targeting these mechanisms of immunosuppression may improve the immunotherapy outcome for AYA melanoma patients.

Ab#009 The role of KDM6A in melanoma

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Melanoma is an aggressive form of skin cancer and Australia has one of highest incidences of melanoma in the world. Current treatments for metastatic melanoma are plagued by the resistance melanomas develop against immunotherapies and targeted therapies. Lysine demethylases (KDMs) are epigenetic enzymes that remove methyl groups from the amino acid lysine (K) on histone proteins, which effects gene expression. One of these KDMs is KDM6A (an X-linked gene also known as UTX) that removes methyl groups from histone 3, lysine number 27 (H3K27me3) inducing activation of gene expression. KDM6A has been reported to play roles in the progression of multiple cancers, however the role of KDM6A in melanoma is yet to be investigated.

In this study, the effects of KDM6A expression on clinical parameters, including survival, and gene expression patterns was investigated in a cohort of 458 melanoma patients obtained from The Cancer Genome Atlas (TCGA). In addition, the effects of KDM6A knockout using the CRISPR-Cas9 system in melanoma cells was investigated using in vitro cell biology assays.

Results showed that high KDM6A expression was associated with better overall survival in melanoma patients, particularly in females but not in males. KDM6A expression significantly correlated with gender in melanoma patients. High KDM6A expression was associated with upregulation of interferon pathways and downregulation of pro-survival pathways which may prevent melanoma growth. High KDM6A expression was also associated with multiple immune cell subsets in melanoma patients, especially in females. KDM6A knockout in melanoma cells significantly increased proliferation and colony formation, hence promoting melanoma cell growth. RNA-seq analysis in KDM6A depleted cells showed significant upregulation of oncogenic pathways and downregulation of tumour suppressive pathways.

These results suggest that KDM6A appears to have a protective effect in melanoma patients, especially in females, indicating a potential tumour suppressive role. Furthermore, KDM6A knockout increased proliferation and colony formation in melanoma cells, further supporting the tumour suppressive role of KDM6A in melanoma.

Ab#010 Integrated Mapping of the Ductal Carcinoma In Situ Ecosystem to Predict Disease Outcome

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Widespread mammographic screening of women over 50 has resulted in remarkable improvements in quality of life and long-term survival from breast cancer due to detection of tumours when they are at an earlier stage. However, this has resulted in a dramatic increase in the detection of ductal carcinoma in situ (DCIS), the non-invasive precursor of invasive ductal carcinoma (IDC), which is confined to the ducts surrounded by a normal myoepithelial cell layer, and may otherwise have gone undetected. Approximately 30% of untreated cases progress to IDC. There is a lack of tools to accurately predict invasive progression, thus virtually all DCIS is surgically removed. Furthermore, most DCIS patients receive radiotherapy after surgery to reduce likelihood of recurrence. This is substantial overtreatment of DCIS patients. Emerging evidence has revealed that the adjacent microenvironment becomes progressively altered in DCIS and IDC compared to normal tissue, and that these changes are correlated with recurrence or progression to invasive disease. To explore this, we measured a panel of myoepithelial markers in a cohort of low and high grade DCIS, with or without association with invasive breast cancer, with extensive clinical follow-up. Progressive loss of myoepithelial cell markers in DCIS tissue was associated with disease progression, suggesting that marker loss predicts long-term outcome. To extend this finding, we are using imaging mass cytometry to characterise a range of microenvironment cell types in our DCIS cohort. This analysis will allow us to characterize spatial relationships between cell types, and relate those relationships to disease outcome. We will identify the interaction between positional relationships and marker changes, to identify patterns that predict outcome. This study has the potential to provide novel biomarkers to assist clinical management and reduce over-treatment of DCIS patients.

Ab#011 The microbiome in bowel polyps

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Background
Bowel polyps are areas of benign but excessive proliferation of bowel epithelial cells. However, approximately 5% of polyps become malignant. Current guidelines for surveillance of polyps employs histological risk factors and family history, without considering the underlying genetic and environmental factors driving polyp transformation to cancer. An increasing body of research has correlated different microbiota with more established, malignant bowel cancers. However, less is known about potential differences in microbiota composition at the gut mucosa between those with early polyps and those without.

Aim
This study aims to parse differences in the gut mucosa microbiome between those with and without polyps to identify bacterial biomarkers that may influence polyp progression into malignancy.

Methods
Biopsies were collected from participants undergoing colonoscopy either adjacent to bowel polyps or from the distal colon in patients without polyps. DNA extracted from these biopsies underwent 16S rRNA sequencing and bioinformatics processing with QIIME2. Differential expression analysis with LefSe parsed microbial differences from cases with and without polyps. Supervised learning methods identified potential microbial biomarkers that could predict these two groups. PiCRUST2 identified potential functional differences between cases with and without polyps.

Results
We analysed 39 cases with polyps with 39 age- and gender- matched healthy cases. There were no differences in alpha diversity between cases with and without polyps. We found small but statistically significant enrichment of bacteria associated with Megamonas, Fusobacterium Varium, Tissierellales and Megasphaera in cases with polyps compared to healthy controls. Bacteria associated with Lachnospira, Coprococcus comes, Christensenellaceae and Eubacterium were typically depleted in cases with polyps compared to healthy controls.

Conclusions
These findings suggest that there are species of bacteria that show subtle differences in abundance between those with and without polyps in the bowel mucosa, and may constitute potential biomarkers for early prognosis of increased bowel cancer risk.

Stream 1.3: Cell biology and immuno-oncology (part 1)

Ab#012 ECM and its novelty in tumor progression

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Tumor progression and its functionality are widely controlled by the local environment within the cell, called the extra-cellular matrix (ECM). This non-cellular component is constantly degraded and remodeled to act as a pro- or anti-tumor factor in tumorigenesis. Recent studies have targeted the ECM to deeply understand the role and pathways underlying this change in tissue organization under varied circumstances. The morphological transition of the cells reflects the importance of ECM in target therapy. In this study, we have studied the role of ECM as a protective milieu during the response of carcinoma cells to therapy. We used ovarian cancer cells (AOCS 15) and squamous cell carcinoma (SCC25) to identify dynamic response patterns in response to chemo and radiotherapy, respectively with and without ECM derived from human dermal fibroblasts (HDF) to help achieve therapeutic strategies with improved clinical outcomes. Another adjunct to this study has been observed using wild-type mouse tongues by completely decellularizing them leaving only the ECM scaffold behind. Further investigations are being carried out to perceive the modifications brought within and by ECM to the seeded tumorigenic m-cherry SCC25 cells visualized under a fluorescence microscope post-immunohistochemistry. This study further focuses on the mechanisms involved in bringing these characteristic evolutions to these tumor cells to help survive against all therapies.

Ab#013 Anti-Tumor Activity of Nimotuzumab and Trastuzumab Antibody Functionalized Gold Nanoparticles as a Potential Immunotherapeutic Agents Against Skin and Lung Cancers

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Recent advancements in nanotechnology have sparked a growing interest in nanoparticle research, particularly in its medical applications. Nimotuzumab is a human epidermal growth factor receptor (EGFR) monoclonal antibody (NmAb) and Trastuzumab is a human epidermal growth factor receptor-2 (HER-2) monoclonal antibody (TmAb) are used for the treatment of EGFR+ and HER-2+ skin and lung cancers. Monoclonal antibody (mAb) has approved and marketed by the U.S. Food and Drug Administration (FDA) for target binding on the specific receptor surface of tumor cells while significant targeting EGFR and HER-2 positive receptors and has had limited success to date. However, the human epidermal growth factor receptor (EGFR/HER) family of tyrosine kinases has been implicating in the development and progression of human cancer. Due to the significant similarity protein sequence of both HER-2 and EGFR, individually Nimotuzumab and Trastuzumab, and in combination with gold nanoparticles are progressing to date on targeting and treating cancers. The goal of these efforts is to revolutionize current methods of treatment and treatment strategies. Herein, we focus on engineered an immunoconjugate by combining therapeutic monoclonal antibody, Nimotuzumab and Trastuzumab with pure Gold (AuNPs) nanoparticles surface for specific targeting and synergistic treatments against Calu-3, and A549 lung and A431 skin cancer cells. Numerous physicochemical methods were used to characterize AuNPs-NmAb and AuNPs-TmAb conjugates, including ultraviolet-visible spectrophotometry (UV-Vis), transmission electron microscopy (TEM), dynamic light scattering (DLS), nanoparticle tracking analysis (NTA), and Fourier-transform infrared spectroscopy (FTIR). By using Polyacrylamide Gel Electrophoresis (SDS-PAGE), NaCl-salts, and a biological medium test, we carried out a binding activity and stability analysis, respectively of Nimotuzumab and Trastuzumab. Furthermore, the cytotoxicity potential and cellular uptake of gold nanoparticles by cells were evaluating in vitro by MTT assay, and ICP-MS respectively. Application of AuNPs-NmAb and AuNPs-TmAb to Calu-3, A549 and A431cancer cells significantly decreased the viability of tumor cells compared to Nimotuzumab by itself. Similarly, the cellular uptake of bare AuNPs was markedly increased by 2 to 4-fold after conjugating to Nimotuzumab and Trastuzumab with pure Gold (AuNPs) nanoparticles in both the cell lines. Eventually, for both cells, approximately 100 µg/mL of bare AuNPs appeared to be safe. These findings revealed that AuNPs-NmAb and AuNPs-TmAb functionalized nanoconjugates target and inhibit the proliferation of selective cancer cells.

Ab#014 CD123-targeting Chimeric Antigen Receptor T-cells for treating Acute Myeloid Leukemia

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Background: Chimeric antigen receptor (CAR) T-cell immunotherapy is a novel treatment modality, which has been especially successful against B-cell leukaemia and lymphoma. However, application to other more common haematological malignancies, like acute myeloid leukemia (AML) remains challenging due to the lack of cancer-restricted antigens. However, the interleukin-3 receptor alpha subunit, CD123 is an attractive target as it is overexpressed in AML bulk disease and leukemic stem cells. Here, we report relative activity of three locally developed novel CAR T-cells targeting CD123.

Aim: To generate and test in vitro CAR T-cells targeting CD123-expressing cells as a first step towards clinical application.

Methods: Three CAR constructs were cloned into the PiggyBat transposon/transposase system. CAR constructs were electroporated into T-cells (n=3), then expanded in vitro using irradiated PBMCs and interleukin 15, for 2 weeks. After day 15, CAR T-cells were assayed for CAR expression, exhaustion and memory phenotypes by flow cytometry. CAR T-cell function was determined by cytokine (TNFα, IFNγ) release and calcein-AM cytotoxicity assays upon co-culture with CD123 positive (KG1) or CD123 negative (HEK293) cell lines.

Results: The CD123-specific CAR T-cells expanded on average 58-fold with CAR expression of 72%±24%. Memory and exhaustion phenotype was similar between all the CAR T-cell cultures. 1.9%-9.6% of CAR+T cells released TNFα, while 1.5%-6.5% released IFNγ in response to KG1. Cytotoxicity assays at 40:1 effector : target (E:T) ratio showed a range of specific lysis (29%-42%). Two of CAR constructs effected CD123Pos KG1 lysis significantly more than CD123Neg HEK293.

Discussion: These data demonstrate the feasibility of generating novel anti-CD123 CAR T-cells which will be confirmed in murine models. The successful completion of this project will enable the development of therapies against various AML antigens, extending the clinical benefit provided by this exciting technology.

Ab#015 EGFR trafficking modes involved in cancer resistance to an immunotherapy.

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EGFR trafficking modes involved in cancer resistance to an immunotherapy

Introduction to the health problem: Head and neck squamous cell carcinoma (HNSCC) affects over 600,000 patients worldwide, where 80% are non-responsive or resistant to an immunotherapy, cetuximab. This treatment is the only selective FDA-approved agent for HNSCC, targeting epidermal growth factor receptor (EGFR) which is involved in dysregulated cellular signalling. Studies to identify differences between the endocytic machineries of cetuximab-sensitive and -resistant cancer cells in vitro may pinpoint novel biomarkers responsible for cetuximab-resistance and in turn advance HNSCC treatments.

Body: Clathrin-mediated endocytosis (CME) and fast endophilin-mediated endocytosis (FEME) are 2 endocytic pathways which traffic EGFR from the cell membrane. Whilst CME is dependent on clathrin and dynamin, FEME is clathrin-independent but involves dynamin and endophilin. CME is a well-established route. However, the downstream endocytic mechanisms of FEME remain unknown. Using immunoblotting techniques on KJD cells, a cetuximab-resistant human squamous cell carcinoma (SCC) line, revealed relatively higher amounts of both dynamin and endophilin over a cetuximab-sensitive cell line. Measuring EGFR endocytosis rates revealed KJD internalised EGFR significantly faster than other SCC lines. FEME cargo uptake begins upon receptor activation by high amounts of its cognate ligand. When KJD cells were stimulated with a high EGF ligand concentration immunofluorescence studies showed that EGFR and endophilin colocalised in cells. Reduced EGF uptake was also observed upon dynamin inhibition, but not clathrin inhibition.

Conclusion: The combined characteristics observed in KJD cells relative to 4 other SCC cell lines suggests that EGFR may largely traffic through a clathrin-independent, dynamin-dependent route involving endophilin in these cells. This raises the possibility that the FEME endocytic pathway may be upregulated in KJD cells. Further studies are required to characterise the pathway trafficking EGFR in cetuximab-resistant KJD cells and may help address questions surrounding the endocytic mechanisms of FEME.

Stream 1.4: Cell biology and immuno-oncology (part 2)

Ab#016 Fatty Acid Oxidation is a Minor Substrate Source to the TCA Cycle in Prostate Cancer Cells.

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Background: Prostate cancer is characterised by enhanced fatty acid (FA) oxidation (FAO) and has been proposed to be the predominant bioenergetic pathway. FAO generates ATP by directly supplying reducing equivalents to the electron transport chain and the precursor acetyl-CoA for the TCA cycle. Several studies have shown that targeting carnitine palmitoyltransferase 1, which catalyses the entry of FAs into the mitochondria, reduces cancer cell proliferation and cell viability, and have linked this to reduced ATP production. However, the relationship between the TCA cycle to FA entry, FAO, and cell proliferation remains unclear.

Aim: To quantify substrate selection into the TCA cycle and thereby determine the contribution of FAO in prostate cancer.

Methods: Six prostate cell lines of varying pathophysiology were incubated in 14C-palmitate containing media to measure FAO rate. Cells were incubated in media with substrates replaced with their U-13C forms and extracted for high-resolution metabolic-flux-analyses. All metabolomic studies performed at Sydney Mass Spectrometry.

Results: Prostate cancer cells had greater FAO rates compared to human prostate epithelial cells. High-throughput metabolic flux studies revealed that glucose and glutamine are the major substrate source for the TCA cycle intermediates (25-30% each) in comparison to essential and non-essential FAs of varying saturation and chain lengths (3-5%). Additionally, we observed that when glucose and glutamine are deprived that palmitate incorporation to the TCA cycle increases (5-10%) yet remains a minor source.

Summary and Conclusions: This study provides quantifiable evidence that FAO is not a major input to the TCA cycle in prostate cancer. Our findings suggest enhanced FAO and reduced cancer cell proliferation when FA entry into the mitochondria is targeted in prostate cancer, is not linked to TCA cycle activity. As such, other mitochondrial FA metabolism pathways, such as those involved in membrane homeostasis, likely play important roles in prostate cancer cell viability.

Ab#017 Cell-cycle dependent regulation of non-productive and productive telomere synthesis in cancer cells engaging in Alternative Lengthening of Telomeres

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10-15% of all cancers do not require telomerase to maintain their telomere lengths, and instead use the Alternative Lengthening of Telomeres (ALT) pathway. Patients with ALT-cancers tend to have worse prognosis. There are currently no effective treatment options for ALT cancers, which are enriched in several paediatric tumour types, especially osteosarcoma, glioblastoma and neuroblastoma.
A key feature of ALT cells is the presence of elevated telomere synthesis during G2 and M-phases of the cell cycle. However, the relationship between ALT phenotypes, telomere synthesis and productive telomere lengthening remains unclear. Using cell synchronization techniques, we arrested U-2 OS ALT cells in G2 or M-phase as well as releasing cells into mitosis from G2-arrest. We demonstrate that the increased ALT phenotypes, which include nascent telomere synthesis in ALT-associated PML bodies, during G2 phase is non-productive due to ejection of ECTRs into the cytoplasm during M-phase and lost by the subsequent G1-phase. Instead, we show using DNA fiber analysis that telomere extension or productive telomere synthesis instead occurs specifically during prometaphase. Exacerbation of telomere replication stress, by depletion of FANCM replication fork translocase, leads to a dramatic secretion of nascent ECTRs into the cytoplasm that are lost by the subsequent G1-phase, in the absence of increased telomere extension. We also further confirm a functional role of translesion polymerase, POLH, in initiating telomere extension in ALT. Finally, we show that these effects are specific to ALT but not telomerase-positive cancers.

The significance of this work is that contrary to the previously accepted dogma that telomere synthesis occurs in both G2 and M-phase, we show that productive telomere synthesis occurs in prometaphase. This has major implications for therapeutic targeting of ALT cancers through cell-cycle dysregulation and telomere-targeted therapies. We are currently further investigating mechanisms involved in cell-cycle regulation of DNA synthesis at the telomere.

Ab#018 Comfort eating: macropinocytosis as a resistance mechanism in breast cancer following glutamine transporter knockout.

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Background: Molecular targets for breast cancer therapy are highly sought after, particularly in an aggressive subgroup known as triple-negative breast cancer (TNBC) which is insensitive to hormone therapies. As many breast cancers display dependence on the amino acid glutamine, the glutamine transporter ASCT2 is considered a promising target. However, the activation of alternative nutrient uptake mechanisms such as macropinocytosis, a mechanism of non-specific macromolecule uptake, may give rise to resistance to therapies targeting nutrient transporters.

Aim: To observe the effects of ASCT2 inhibition in breast cancer, and to determine whether macropinocytosis is activated in TNBC following transporter loss.

Methods: CRISPR-Cas9 ASCT2 knockouts (KO) were generated from six breast cancer cell lines. Amino acid uptake and cell viability in each line was examined and compared to matched controls. RNA sequencing (RNA-Seq) analysis was performed on the glutamine-addicted TNBC cell line HCC1806 (control and KO) and compared to HCC1806 ASCT2 shRNA knockdown (KD) lines. To quantify macropinocytosis in HCC1806 lines, uptake of high-molecular-weight dextran molecules was measured by fluorescence microscopy.

Results: In HCC1806 cells, ASCT2 KD markedly inhibited glutamine uptake and cell growth, while cell growth following KO was unaffected. Following KO in five additional breast cancer cell lines, growth was again unaffected in all but one. We proposed that compensatory mechanisms may be activated following KO but not KD. Indeed, HCC1806 ASCT2 KO lines displayed a significant induction of macropinocytosis. Through RNA-Seq, potential drivers of this macropinocytic phenotype were identified – a sorting nexin protein known as SNX33, and a roundabout receptor known as ROBO1.

Conclusion: Contrary to the results of previous RNA interference studies, TNBC and other breast cancer lines are unaffected by loss of ASCT2. This may be attributed to a compensatory elevation of macropinocytosis, and prompts caution when considering this transporter, or nutrient transporters more broadly, as molecular targets.

Ab#019 PTU, a novel inhibitor of Wnt5a-mediated protrusions, inhibits High Grade Glioma cell invasion in 3-dimensional in vitro models

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Background: High Grade Gliomas (HGG) are aggressive brain cancers with limited targeted therapies and dire prognosis. HGG spread is characteristically diffuse, and far-invaded cells are often missed by first-line treatments leading to tumour recurrence. Anti-invasive agents can limit cell spread and improve efficacy of adjuvant anti-cancer therapies; a multi-pronged approach that may circumvent the current absence of successful HGG treatments. PTU (p-toylyl-ureidopalmitic acid) has been demonstrated to suppress invasion in breast cancer via inhibition of Wtn5a-mediated protrusions and is a promising candidate to target HGG invasion.

Aim: As elevated Wnt5a has been associated with invasive and recurrent forms of HGG, and given that PTU is blood-brain-barrier permeant, we have investigated the effect of PTU on the invasion of patient-derived HGG using systems designed to replicate discrete aspects of the 3D in vivo environment of brain cancer.

Methods: PTU was tested in a variety of models, including: 1) multi-cellular spheroids of patient derived HGG cells and patient-derived tumour organoids embedded in a native 3D matrix, 2) single cell suspensions in 3D matrix or printed in RGD-bound poly-ethylene glycol polymer using a 3D bioprinter, and 3) multi-cellular spheroids co-cultured with brain organoids derived from human embryonic stem cells. Additionally, we have undertaken preliminary spatial profiling, comparing quantitative protein expression between regions corresponding to intra-tumoural, peri-tumoural and healthy brain tissue in PTU treated organoid/multicellular tumour spheroid co-cultures using GeoMxTM digital spatial profiling (DSP).

Results: In each model, PTU significantly reduced the invasion of HGG cells in multiple patient-derived cell-lines, while single-cell tracking revealed a reduction in cell speed. Preliminary analysis of DSP showed distinct protein expression profiles in PTU vs vehicle-treated samples across each region.

Summary/Conclusion: As a derivative of Omega-3-polyunsatured-fatty-acids, PTU is expected to have limited side-effects. Our data, using unique biologically-relevant models, suggests that PTU holds great promise as a novel, brain-penetrating, anti-invasive treatment for HGG.

Stream 1.5: Novel treatments

Ab#020 Leptospermum extras suppress malignant pleural mesothelioma tumour growth in vitro and in vivo

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Background: Malignant pleural mesothelioma (MPM) is a highly aggressive cancer induced by past asbestos exposure. MPM has a very poor prognosis and patients are usually short lived. The resistant nature of MPM given limited effective treatment options. Recent published studies highlighted the potential of honey in mesothelioma; however, the in vitro and in vivo response of honey are limited. In this study, we have utilised a specific method to isolate active ingredient from leptospermum, we aim to investigate the anti-cancer property of the leptospermum extract (QV0) in mesothelioma in vitro and in vivo.

Methods: Leptospermum extras (QV0) and honey formula (Defender) is kindly provided by Hon-E-Heaven®. The anti-cancer effects of QV0 were investigated by cell proliferation assay and cell cycle analysis in 13 mesothelioma cell lines. Seahorse mito stress test was conducted to measure mitochondrial function after QV0 treatment. To study the in vivo response of Defender, CBA mice (n=20, female) were injected with 1 X 106 mouse mesothelioma cell line (AC29) with a stable pGL4-51lu construct for luciferase visualisation of tumour grown. Defender (5mg/mouse/20g bodyweight) was administrated via oral gavage as a daily supplement. The tumour size was measured once a week with an IVIS imager that visualisation with luciferin substrate (150mg/kg) for a period of 31 days. Liver toxicity test, glucose tolerance test was performed to evaluate the long-term systemic effects post treatment.

Results: We have demonstrated that QV0 suppressed all 13 MPM cell lines growth in a dose dependent manner, being effective at concentrations as low as 0.02%. This effect is associated with shortened G0-G1 phase of cell cycle and increased maximal oxygen consumption rate post QV0 treatment. Animal treated with Defender demonstrated a reduced tumour size over 31 days. In addition, animal treated with Defend better maintained their body weight after tumour implantation with an average extended life span of 7 days. We analysed liver and spleen collected from animal treated with Defender, result indicated that there is no liver toxicity nor increase in blood glucose concentration post treatment.

Conclusion: We are the first to reported that a specific leptospermum extract (QV0) and its food formulation (Defender) inhibited MPM tumour growth in both cell culture and improve host survival in MPM mice model.

Ab#021 Dual payload ADC approach to target and treat HER2+ breast and colon cancer cells

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Background: Breast cancer is one of the leading causes of death worldwide. Unfortunately, colon cancer follows not too far behind in its mortality rate. Fortunately, there has been a rise in the number of clinical trials against cancer. However, there are various limitations associated with treatment development some of which includes poor tumour penetration and retention as well as acquired drug resistance mechanisms that cancer cells utilise to cleverly evade treatment which thereby hinders the efficacy of ADCs.

Aim: Our objective was to investigate the feasibility of conjugating two payloads to an antibody as well as the synergistic effect of an ADC comprised of dual payloads in vitro, to target the HER2+ antigen in breast and colon cancer cell lines, SKBR3 and DLD-1 respectively.

Methods: The two payloads employed were MMAE and DM1. Both payloads inhibit microtubule polymerisation and were chemically conjugated to amino acid residues (i.e., either cysteine or lysine) on trastuzumab. The ADC was then characterised via UV-Vis spectroscopy, SE-HPLC and other minor experiments to confirm payload conjugation, eliminate the potential for the presence of aggregates and thiol groups respectively. The anti-proliferative effects were observed via cell viability assays.

Results: Our results indicated that the ADC had a synergistic effect against both cell lines and successfully demonstrated a 50% growth rate inhibition in the nanomolar range. However, SKBR3 was more sensitive to the novel ADC than the DLD-1 cell line due to its higher HER2 expression.

Conclusion: The dual payload approach could pave the way to employ other linker-payload moieties to various antibodies to construct dual (or multitudinous) payload complexes. It has the potential to overcome some of the limitations mentioned above as each linker-payload moiety employed can either target both microtubules polymerisation and DNA or just one to ensure complete cell death and apoptosis.

Ab#022 Peptide-based inhibitors for targeting telomerase-active cancers

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Telomeres are important nucleoprotein structures capping the ends of chromosomes that act as a form of protection against DNA replication errors. However, telomere attrition is inevitable with each iteration of chromosome replication, resulting in replicative senescence and eventual cell death. Cancers have developed methods to maintain their telomeric DNA in order to avoid cell death from replicative limitations. Many cancers, such as lung cancers and glioblastoma, upregulate the expression of the telomerase holoenzyme to repair degraded telomeres and bypass these limitations, allowing them to proliferate indefinitely. Recently, the DBHS family of proteins have been implicated in the assembly of the active telomerase core complex.

In this presentation, we report our investigations towards peptide-based inhibitors against the DBHS family of proteins. We identified a candidate 16-mer partially helical peptide, P01, by screening peptide fragments from the dimerisation domain of NONO, a member of the DBHS family. Subsequently, a double cysteine mutant for P01 was designed for stapling, and a series of side-chain cyclisation linkers were tested to determine the effect of the linker moiety on binding. Interestingly, an increase in binding was observed upon mutating two residues into cysteines, while cyclisation with many of the helix-matching linkers resulted in loss of binding.

In addition, we also report the results of alternative screens against NONO, including fragment screening and various display approaches to cyclic peptide screening.

Ab#023 Developing Renal Clearable Nanoparticles For The Treatment Of Renal Cell Carcinoma

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Renal Cell Carcinoma (RCC) pose a great burden to global public health as current therapies are generally ineffective. Nanoparticles (NPs) have become a platform for targeted drug delivery in the treatment of various diseases & cancers. NPs with large size (>10 nm) or heavy metal components have significant concerns regarding long-term organ toxicity, limiting their clinical translation. Renal clearable NPs with size <6 nm can be excreted via kidneys and have great potential to decrease systemic toxicity by avoiding accumulation in healthy tissues/organs after systemic administration. We successfully developed novel NPs (carbon dots, CD) with size less than 6nm possessing renal clearable properties as a vehicle to carry drugs and inhibitors for specific targeting of RCC. The effect of drug and its conjugates was assessed initially in vitro by MTT Assay after 24 and 48 hr treatment. These CDs were shown to have very low cytotoxicity at concentrations up to 200ug/ml; possess high quantum yield (58%) with bright blue fluorescence observed under UV light; drug loading capacity for hydrophilic and hydrophobic compounds. The excitation-dependent photoluminescence properties allowed visual monitoring of the cells in blue, green and red fluorescence channels. The cell viability assay in Renca cells demonstrated that CDs carrying doxorubicin (CD-DOX) significantly reduced the viability of the Renca cells compared to free DOX (P value=0.0167). In Hela cells, the cell viability was also reduced with CD-DOX compared to free DOX (P value=0.0068). The in vivo study is in progress. In conclusion, the CD conjugated drug shows better inhibition of growth in cancer cell lines compared to the unbound chemotherapeutic, suggesting that these nanoparticles have therapeutic potential in RCC.

Ab#024 Off the Shelf Chimeric Antigen Receptor T-cells for Malignancy: A nonviral and site-specific approach

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Background: Chimeric Antigen Receptor (CAR) T-cells are genetically modified T-cells expressing an artificial receptor that enables them to target and lyse cancer cells. CAR T-cells 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, CAR T-cells are currently manufactured individually for each patient from autologous T-cells. This individualised production process is time-consuming and expensive, costing >$500,000AUD per product. Furthermore, most CAR T-cell therapies in the current clinical landscape use random gene integrating viral or non-viral techniques to insert the CAR transgene, with a potential risk of insertional mutagenesis.

Aim: To overcome these hurdles, we aim to generate Off the Shelf CAR T-cells using site-specific gene-integrating tool, CRISPR/Cas9, to knock-out the T-cell receptor (TCR) complex, thereby markedly reducing the cost and enabling their universal use.

Methods: T-cell transfection by electroporation was performed with CRISPR/Cas9 and homology-directed repair templates on healthy 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 following electroporation.

Results: Preliminary data demonstrates that using two single guide RNA and short homology arm length is sufficient to achieve up to 80% knock-out of TCR and up to 35% knock-in of CAR. These CRISPR CAR T-cells exhibit comparable expansion, memory phenotypes and expression of immunoinhibitory molecules to our Phase I clinical trial CAR T-cells produced with nonspecific integration techniques.

Summary/Translational Significance: Our data demonstrate that alternative precise, cutting-edge technologies can be used to generate novel and safer anti-tumour CAR T-cells that can be translated into effective therapeutic options. This developmental research will lay the crucial groundwork for the development of future cell therapy products to target various malignancies.

Ab#025 A new strategy to overcome Triple-Negative Breast Cancer metastasis: combining novel targeted therapeutic candidates with an anti-Breast Cancer Associated Fibroblast agent

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Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer mortality in women worldwide. Triple-negative breast cancer (TNBC) is an aggressive form, which accounts for 15-20% of breast cancer. There is a lack of effective targeted therapeutics for TNBC as it does not have common estrogen, progesterone and HER2 receptors, so non-specific chemotherapy is the main method of treatment. Often chemotherapeutic treatment leads to various side effects, which limits dosage and prevents from administering dosage that could completely eradicate the cancerous cells. In some cases, the disease often reoccurs or relapses after an initial successful response. A major contributor to this survival of disease is breast cancer associated fibroblasts (BCAFs), which assists with tumour growth, progression, invasion and metastasis. Hence, TNBC is considered an unmet medical condition that urgently needs novel effective therapeutics. Aims: The aims are to determine the efficacy of the novel peptide-based drug conjugate in combination with a secondary anti-BCAF agent, in TNBC spheroids and co-cultures of spheroids and BCAFs. Methods: TNBC spheroids will be developed in a microwell scaffold. The combination therapy will be tested in a co-culture of BCAF and TNBC spheroids in a 3D microfluidic cell culture device. The efficacy of treatment for TNBC will be assessed by cell viability assays, uptake of compounds and migration and invasion assays using confocal microscopy. Significance: This project could lead to the development of potent and selective anticancer pharmaceuticals, which will improve TNBC cancer patients' survival and quality of life by reducing side effects.

Stream 2.1: Quality of life

Ab#026 Assessment of Chemotherapy-Induced Peripheral Neuropathy- A comparison of clinical, functional and patient reported approaches

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Introduction: Chemotherapy-induced peripheral neuropathy (CIPN) is a significant toxicity of numerous chemotherapies that significantly impacts cancer survivor's long-term quality of life. Early identification of CIPN is crucial in preventing long-lasting nerve damage. However, this is complicated by a lack of a gold-standard CIPN outcome measure. This study aimed to evaluate the validity and responsiveness of different approaches to CIPN assessment in order to identify optimal outcome measures.

Methods: 859 cancer patients (54±13 years) treated with various neurotoxic chemotherapies (taxanes, platinums, vinca-alkaloids, bortezomib, immunomodulatory drugs) underwent comprehensive nerve assessment with patient reported outcome measures (PROMs; EORTC QLQ-CIPN20, FACT/GOG Ntx-13 and PRO-CTCAE), clinical grading (National Cancer Institute NCI grade, Total Neuropathy Score (TNSc), nerve conduction studies) and sensory functional measures (monofilaments, 2-point discrimination, grating orientation, grooved pegboard). Convergent validity was assessed with Spearman's correlation coefficient of >0.7 between each measure and NCI grade. Discriminant validity compared measures using t-tests between NCI grade ≤1 (non-significant) and grade ≥2 (significant) CIPN. Responsiveness was evaluated in 356 patients who were prospectively assessed, comparing pre-treatment to mid-treatment scores with effect sizes (ES).

Results: PROMs demonstrated convergent validity with high correlations to NCI grade (r=0.74-0.88, P<0.01). Sensory functional measures and other clinical grading scales did not achieve acceptable correlations (all r<0.7, P<0.01). Discriminant validity was demonstrated in all measures, indicating all measures were able to differentiate between non-significant and significant CIPN (all P<0.01). PROMs were the most responsive outcome measures (ES=0.63-1.63). Sensory functional measures and other clinical grading scales did not demonstrate high responsiveness (ES=0.06-0.27) except for the TNSc, a composite neurological grading scale (ES=1.04).

Conclusion: PROMs demonstrated superior validity and responsiveness compared to clinical grading and sensory functional measures of CIPN. This present series suggests the use of PROMs in combination with a responsive objective measure such as the TNSc provides most optimal evaluation of CIPN.

Ab#027 Priority Recommendations for the Implementation of Patient Reported Outcomes in Clinical Cancer Care: A Delphi study

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Purpose: The aim of this study was to develop priority recommendations for the service level implementation of patient reported outcomes (PROs) into clinical cancer care.

Methods: Development of draft guidance statements was informed by a literature review, the Knowledge to Action (KTA) implementation framework, and discussion with PRO experts and cancer survivors. A two-round modified Delphi survey with key stakeholders including cancer survivors, clinical and research experts, and Information Technology specialists was undertaken. Round 1 rated the importance of the statements and round 2 ranked statements in order of priority.

Results: Round 1 was completed by 70 participants with Round 2 completed by 45 participants. Forty-seven statements were rated in Round 2. In Round 1, highest agreement items (>90% agreement) included those that focused on the formation of strong stakeholder partnerships, ensuring ongoing communication within these partnerships, and the use of PROs for improvement and guidance in clinical care. Items ranked as the highest priorities in Round 2 included assessment of current staff capabilities and service requirements, mapping of workflows and processes to enable collection, and using collected PROs to guide improved health outcomes.

Conclusions: This study stands as the first of its kind in formulating stakeholder derived recommendations and a practical guide to implementing PROs in the cancer care clinical context. This work can be viewed as a building block from which health services can guide their considered efforts for PRO implementation while considering their local context. The stakeholder consultation process identified key priorities in PRO implementation into clinical cancer care that include: clinical relevance, stakeholder engagement, communication, and integration within the existing processes and capabilities. Routine adoption of PRO collection by clinical cancer services requires multiple implementation steps; of highest priority is strong engagement and communication with key stakeholders including cancer survivors.

Ab#028 Prophylactic use of compression sleeves reduces the incidence of arm swelling in women at high-risk of breast cancer-related lymphoedema: a randomised controlled trial

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Purpose: To determine whether prophylactic use of compression sleeves can prevent arm swelling in women at high risk for breast cancer-related lymphoedema (BCRL).

Methods: Women (n = 307) who had undergone axillary lymph node dissection were randomly assigned to either a compression or control group. In addition to usual postoperative care, participants in the compression group were provided with two compression sleeves to wear from the first postoperative day until three months after completing adjuvant treatments. Arm swelling was determined using bioimpedance spectroscopy (BIS) thresholds and relative arm volume increase (RAVI) separately. The incidence and time free from arm swelling were compared using Kaplan-Meier analyses. Hazard ratios were estimated from univariate and multivariate Cox regression models for BIS and RAVI thresholds independently.

Results: The hazard ratio for developing BCRL in the compression group relative to the control group was 0.61 (95% CI: 0.43 to 0.85; p = 0.004) based on BIS and 0.56 (95% CI: 0.33 to 0.96; p = 0.034) based on RAVI. The estimated cumulative incidence of arm swelling at one year was lower in the compression group than the control group based on BIS (42% vs. 52%, respectively) and based on RAVI (14% vs. 25%).

Conclusions: Prophylactic use of a compression sleeve compared to the control group reduced and delayed the occurrence of arm swelling in women at high risk for BCRL in the first year after surgery for breast cancer.

Keywords: breast cancer-related lymphoedema, compression sleeve, prevention

Ab#029 Prevalence of concerns in Indian Head and Neck Cancer (HNC) populations reported on the Patient concerns Inventory (PCI): A brief report

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Background: There are approximately 200,000 new cases of head and neck cancer (HNC) annually in India. The anatomy and nature of HNC treatment impacts a person's function, appearance and socialization. With treatment advances, more HNC patients live longer with some degree of need for monitoring and support. This study aims to explore the primary concerns of Indian HNC populations speaking three languages – Tamil, Telugu or Hindi.

Methods: Three tertiary cancer centres in India participated. Eligibility criteria included HNC diagnosis (excluding thyroid cancer), any cancer stage, in treatment or follow-up, and aged 18 years or older. Consenting participants completed the Patient Concerns Inventory (PCI). We calculated the response rate (percentage of patients who responded 'yes' or 'no') for each concern on the PCI across language groups.

Results: Participants included 621 HNC patients (Tamil = 205, Telugu = 216 & Hindi = 200). Of the 56 concerns, Telugu (28/56) and Hindi groups (27/56) reported the largest number of concerns. Patients' concerns were highest in the treatment-related domain (100%), followed by physical and functional well-being (72%). Fear of cancer recurrence was reported by 98.5% Telugu patients, 47.5% Tamil, and 34% Hindi.

Conclusion: HNC patients in India have a high number of concerns. There are both similarities and differences in concerns across the three language groups. Responses indicate PCI is acceptable and sensitive to the concerns of Tamil, Telugu and Hindi speaking HNC patients in India. Future research should address the concerns identified to improve the overall health-related quality of life in these patients.

Ab#030 Palliative Paramedicine: Comparing Clinical Practice through Guideline Quality Appraisal and Qualitative Content Analysis

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Background: Palliative care is an emerging scope of practice for paramedicine that facilitates community preferences to live and die at home. Cancer patients spend 90 percent of their last years of life at home and, despite meticulous planning, deterioration usually occurs out-of-hours. The COVID-19 pandemic has highlighted the opportunity for paramedics to deliver palliative and end-of-life care to patients wishing to avoid intensive life-sustaining treatment, especially after hours, and support home-based death. However, a gap remains in understanding the provision and limitations of current ambulance services' pathways of palliative and end-of-life care.

Aim: To examine the quality and content of existing palliative paramedicine guidelines across Australian and comparable international ambulance services.

Methods: We appraised guideline quality using the AGREE II instrument and employed a collaborative qualitative approach to analyse the content of the guidelines.

Results: None of the guidelines were recommended by both appraisers for use based on the outcomes of all AGREE II evaluations. Scaled individual domain percentage scores varied across the guidelines: scope and purpose (8% to 92%), stakeholder involvement (14% to 53%), rigour of development (0% to 20%), clarity of presentation (39% to 92%), applicability (2% to 38%), and editorial independence (0% to 38%). Six themes emerged from the content analysis: (1) audience and approach; (2) communication is key; (3) assessing and managing symptoms; (4) looking beyond pharmaceuticals; (5) seeking support; and (6) care after death.

Summary/Conclusion: Palliative care is a growing provision of paramedicine and translated into practice by ambulance services' palliative and end-of-life care guidelines. Future research should explore the experiences and perspectives of key palliative paramedicine stakeholders to inform prospective guidelines; the methodological development of which should follow the AGREE II criteria to achieve best practice.

Stream 2.2: Psycho-social

Ab#031 Supporting breast cancer survivors via text messages: Reach, acceptability, and utility of EMPOWER-SMS

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Background: Five-year survival rates after breast cancer diagnosis are high (91%). Recovery from treatment can negatively impact mental and physical health, and there is limited accessible support. Text messages are an accessible and scalable strategy to deliver health support. However, there was limited evidence for breast cancer survivors' perceived usefulness, acceptability, and engagement with a lifestyle-focused text message intervention.

Aim: Evaluate the reach, usefulness, acceptability, and factors influencing engagement with a lifestyle-focused text message intervention called 'EMPOWER-SMS' to support women's mental and physical health after breast cancer treatment.

Methods: Mixed-methods evaluation nested in the EMPOWER-SMS randomised controlled trial (n=160; intervention n=80, wait-list control n=80). Inclusion: Adult (>18 years), finished active treatment (surgery, chemotherapy, radiotherapy), own a mobile phone, provide informed consent. Exclusion: Metastatic diagnosis. Data sources: screening logs, text message delivery software analytics, intervention feedback survey and focus groups (n=16; summarised thematically using Framework approach).

Results: Women (N=387) met the inclusion criteria (meanage±SD=59.3±11.6 years). Participants who were excluded/declined (n=227) were significantly older than those who enrolled (62.2±11.1 vs 55.1±11.1 years, respectively, p<0.001). Most participants (64/80; 80%) completed the end-of-study survey, reporting the messages were easy-to-understand (64/64; 100%), useful (58/64; 91%) and motivating (43/64; 67%). Focus groups (n=16) revealed factors influencing engagement: i) feelings of support/continued-care ii) messages delivery convenience/flexibility iii) weblinks iv) credible information sources and v) options to save/share messages.

Conclusion: A lifestyle-focused text message program was acceptable and useful for women after breast cancer treatment. However, text messaging may be a barrier for women aged over 68years. Suggestions for program improvements included delivering the program to patients with other cancers, during all stages of treatment and including more weblinks in text messages.

Implications for cancer survivors: An acceptable and useful low-cost strategy to deliver post-treatment health support in a non-invasive way and potentially facilitate patient-health professional communication.

Ab#032 A systematic review and meta-synthesis examining fear of cancer recurrence in informal caregivers

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Background: Caregivers play an important role in supporting cancer survivors. Whilst fear of cancer recurrence (FCR) has been reported by both survivors and caregivers, few studies have investigated FCR in caregivers. We aimed to review and meta-synthesise research examining FCR in caregivers. Specifically, we sought to determine (a) whether FCR in caregivers conceptually differed to FCR amongst survivors; and (b) the utility of caregiver-specific measures of FCR in capturing caregiver FCR. On the basis of these findings, we aimed to develop a hypothesis-generating model of caregiver FCR to inform future theoretically-grounded research examining caregiver-specific FCR.

Methods: Four databases were searched. Eligibility criteria included English language, peer-reviewed journal articles published between January 1997 and July 2021. Two researchers reviewed article eligibility; data was extracted, and quality appraisal conducted. To evaluate the psychometric properties and content of FCR measures the COSMIN taxonomy was used.

Results: A total of 46 texts were included. Meta-synthesis revealed 2 themes uncertainty/fear and caregiver's role as protector, which was unique to the caregiver experience. An overarching theme, fear of losing a loved one, was a driver of FCR. Various instruments measured FCR in caregivers, most using adapted patient instruments (n=24). Four studies used scales developed specifically for partners/caregivers.

Conclusion: Similarities exist between survivor and caregiver FCR, however there are important elements to caregiver FCR that differ conceptually to the fear experienced by cancer survivors. We propose a model of caregiver FCR which provides an important foundation for future research examining FCR in caregivers. Furthermore, there is a need for measures which capture differences between survivors and caregivers.

Ab#033 Acceptability of an Evidence-Based Booklet for HPV-Related Oropharyngeal Squamous Cell Carcinoma Patients and their Partners

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Introduction: The Human Papillomavirus (HPV) is well recognised as a factor in developing oropharyngeal squamous cell carcinoma (OSCC). We designed an evidence-based booklet for HPV-related OSCC patients, informed by interviews with health professionals, patients and their partners. It aimed to deliver evidence-based messages in everyday language, in a way to minimise negative psychological impacts on patients. Here we aimed to explore the suitability of the booklet for use in Australia and New Zealand.

Methods: Participants were recruited through social media (Twitter, Facebook), provided informed consent and were interviewed via Zoom. Participants were shown the booklet and a Think Aloud method elicited real-time reactions to the content. Responses were analysed for each section and coded as either for or against for content, with other responses thematically analysed using NVivo.

Results: The sample comprised 24 participants, all patients who participated (n=19) had completed treatment for HPV-related OSCC. Partners and friends of survivors of HPV-related OSCC also participated (n=5). All participants found the booklet useful and a large proportion wished the resource had been available previously. Some indicated some information was new to them. The majority agreed the booklet would be best delivered by their specialist at point of diagnosis and would be a useful resource for friends and family. Most participants gave feedback on improvements to the booklet in terms of comprehension and design. Overall, the booklet was well received, and participants found the content easy to understand. Most participants found it helped to reduce shame and stigma associated with HPV as a sexually transmitted infection.

Conclusions: An evidence-based booklet for HPV-related OSCC patients and their partners is acceptable. Implementation may be feasible in routine clinical practice, specifically at time of diagnosis. Responses to the content will help optimise the efficacy of the booklet in facilitating communication between all stakeholders.

Ab#034 Psychosocial and quality of life experiences of people with advanced colorectal cancer: A mixed-methods study

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Background: Approximately 18% of patients with colorectal cancer (CRC) are diagnosed with advanced cancer, while 30-40% develop recurrent disease after treatment with curative intent. Survival from advanced colorectal cancer (CRC) can be prolonged through treatments including: cytoreductive surgery and hypothermic intraperitoneal chemotherapy (CRS-HIPEC), pelvic exenteration, liver resection, and palliative chemotherapy without surgery. Qualitative research into survivors' experiences and needs of people receiving these treatments is lacking.

Aim: This study, through a mixed-methods design, aims to examine and compare the experiences and needs of people who receive different treatment(s) for advanced colorectal cancer.

Methods: Adult CRC survivors who have undergone the aforementioned treatments were recruited 0.5-2 years post-surgery (or 0.5-2 years post-diagnosis of advanced CRC for palliative chemotherapy participants). Quantitative data collected included demographic and clinical data, Functional Assessment of Cancer Therapy – Colorectal (FACT-C), Distress Thermometer, and Comprehensive Score for Financial Toxicity (COST). Participants completed a qualitative semi-structured telephone interview exploring quality of life, employment, finances, supportive care needs, social functioning, and impacts of COVID-19. Interviews underwent framework analysis, guided by quantitative scores.

Results: Analysis of 38 interviews (n=10 pelvic exenteration, n=9 liver resection, n=7 palliative chemotherapy, n=6 CRS-HIPEC, n=6 liver resection + CRS-HIPEC) revealed that treatment for advanced CRC may result in side effects that limit survivors' physical functioning, and can impact psychosocial wellbeing, sense of identity, and ability to work. Participants reportedly manage these challenges through distraction, positive reframing, and connecting with other CRC survivors. Most participants expressed satisfaction with their healthcare experiences. COVID-19 telehealth consultations were considered less personal, but convenient.

Conclusions: Advanced CRC survivors face unique challenges that impact several domains of their lives. Improved care co-ordination and monitoring of symptoms throughout follow-up is needed to better support advanced CRC survivors.

Ab#035 Stakeholder perspectives on the impact of COVID-19 on oncology services: A qualitative study.

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Aim: In response to COVID-19 cancer services in Australia adapted quickly to reduce infection risks for staff and patients, while maintaining an appropriate level of cancer care. This study, conducted by the Psycho-oncology Co-operative Research Group (PoCoG), aimed to document changes to oncology care in Australia, and the impact of the changes on Australians living with cancer, family carers, and Oncology health professionals.

Methods: A longitudinal mixed methods study involving three short surveys and semi-structured telephone interviews over 12 months was conducted. Stakeholders were asked to reflect on their experiences and perceptions of the impact of COVID-19. Demographic and clinical characteristics were elicited and psychological wellbeing assessed. Interviews were thematically analysed using a framework approach.

Results: Seventy eight stakeholders (32 patients, 16 caregivers and 30 HPs) completed baseline interviews, 52 completed (23 patients, 10 caregivers, 19 HPs) 6 month interviews and to date 25 (9 patients, 4 caregivers, 11 HPs) 12 month interviews have been completed. Across timepoints thematic analysis identified three themes related to the emotional impact of COVID-19 as common to all groups: perceived risk, uncertainty, and isolation. Four change themes were also common to all groups: safety, increased stress and loss of support, communication challenges and gains, including information access and communication quality; and quality of care. Safety was a paramount concern. HPs worried patients and carers were prioritising COVID-19 safety over seeking appropriate care for cancer symptoms and the long term impact of this. Patients and carers felt reduced support was available. HPs found telehealth and COVID-19 communication took up more time and the information overload was exhausting.

Conclusion: Changes made to cancer services in response to COVID-19 left many feeling excluded, or ill-informed, and for some, a sense that quality of care had been impacted. While health service changes were deemed necessary and effective in controlling the risk of infection, it is vital that we return to pre-COVID-19 service levels as soon as possible.

Ab#036 Experiences and perspectives of cancer patients/survivors, carers, cancer care healthcare professionals, and non-government cancer services, regarding COVID-19 vaccination

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Background: The risk of dying from COVID-19 is higher for those who are older, immune-compromised, or chronically ill. Vaccines are an effective strategy in reducing mortality and morbidity from COVID-19. However, for the COVID-19 vaccination program to reach its full potential, vaccines must then be taken up by those at greatest risk. Cancer patients are one such vulnerable group. Understanding the perspectives of cancer patients, carers, cancer care healthcare professional (HCP), and non-government cancer services (NGO) regarding COVID-19 vaccination will be critical to ensuring appropriate support and information is provided to facilitate vaccination of this vulnerable group.

Aim: The aim of this research is to explore cancer patient, carer and cancer care healthcare professional (HCP), and non-government cancer services (NGO) views on COVID-19 vaccination.

Methods: Fifty-nine semi-structured interviews were conducted with cancer patients (n=23), carers (n=10), HCPs (n=19) and representatives of NGOs (n=7) across Australia. Transcripts were thematically analysed, using an inductive approach.

Results: Cancer patients, carers, HCPs and NGOs expressed mostly positive attitudes towards COVID-19 vaccination. The following key themes were identified across all participant groups: 1. High motivation - COVID-19 vaccination perceived as offering health protection and hope (with a minority hesitant and some concerned about vaccine hesitancy among the general population); 2. Confusion and frustration - regarding vaccine rollout and communication about cancer patient eligibility; 3. Ongoing uncertainty - about access to vaccine and long term vaccine efficacy; 4. Desire for expert, individualised advice - on vaccine interaction with cancer treatments; and 5. Perceived lack of choice - regarding which vaccine was accessible.

Conclusion: These findings point to the COVID-19 vaccine concerns and information needs of key cancer stakeholders. Policymakers need to provide clear tailored information regarding vaccine eligibility and accessibility to facilitate vaccine uptake.

Stream 2.3: Imaging, radiology and surgery

Ab#037 A model to predict the lifetime dose and allocate a dose category from a single screening mammographic event

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This project aims to devise an innovative approach to establish a dose model that aims to evaluate the total lifetime radiation dose received by a women undergoing any combination of routine screening mammography, that will also be used to allocate women to a particular dose category, all using information obtained from one screening event. A Cancer Institute NSW South Wales (CINSW) dataset containing 30,562 mammograms from 7,595 exami¬nations of women aged between 40-75 years of age was used to establish the model prototype. Preliminary results demonstrate a lifetime cumulative dose of 49.8 mGy, 70.2 mGy and 95.2 mGy for a low, average and high risk woman, respectively, for biennial screening from 50 to 74 years. This unique tailored approach will empower women and clinicians enabling a more in¬formed discussion regarding the benefits and risks of the screening process. It will also inform health policy makers who are considering the possible introduction of alternate screening durations and intervals. The pro¬posed model will ultimately be available as an on-line platform that will be made accessible to all women, doctors and health policy makers free of charge.

Ab#038 A systematic review reporting the computerised quality control of mammography phantom images

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Background: Quality control of mammography images is typically performed by expert human observers using physical phantoms with embedded test objects, mimicking tumours, microcalcification and fibrous structures, in order to ensure that the mammography system produces high-quality images with minimum radiation dose in the clinical setting. Human evaluation inherently tends to be subjective and can be affected by external factors such as viewing conditions, expertise level, and fatigue. However, computerised analysis may enable objective, reproducible, and quantitative evaluation of quality control images.

Objective: To systematically reviewing the benefits of using computerised image analysis to evaluate image quality of mammographic images in comparison to human observers, as well as the algorithms and techniques used in the computerised assessments.

Methods: Studies comprised automated or semi-automated image analysis to assess the two-dimensional (2D) mammography images of physical phantoms were included. MEDLINE, EMBASE, CINAHL, Scopus, and Web of Science databases were searched up to July 2020 using a broad search strategy to include all potentially relevant journal articles and full-text conference papers that were published in English.

Results: Twenty-six studies met the inclusion and exclusion criteria, with the images analysed being either digital images (n=12) or digitised screen film images (n=14). The most frequently used phantom in the studies was the former American College of Radiology (ACR) phantom (n=11). While the image analysis methods used in the included studies varied, they mostly present excellent agreement with the human observers' assessments and eliminated the intra- and inter- observers' variation. Even though, several algorithm methods had low capability in distinguishing low contrast objects compared to the high contrast objects.

Conclusions: The computerised image quality assessment provides objective and reproducible results compared to the subjective human assessment. Additionally, it helps identifying subtle changes in the mammography system's functionality that may affect image quality.

Ab#039 Varying Performance Levels for Diagnosing Mammographic Images Depending on Reader Nationality Have AI and Educational Implications.

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The performance of radiologists in reading mammography is essential in breast cancer detection and survival. This study investigated whether radiologists from different countries share the same sensitivity to certain mammographic features. Retrospective data were collected from Chinese and Australian radiologists reading a high-density test set which contained 40 normal and 20 cancerous mammographic cases. Sixteen Australian radiologists, and 30 Chinese radiologists, including 18 from Nanchang and 12 from Hong Kong SAR/Shenzhen, were asked to read all images in this test set using the Royal Australian and New Zealand College of Radiologists (RANZCR) rating system and annotate the suspicious lesion(s). For each case and each radiologist group, the percentage of radiologists making the correct diagnoses was calculated. For cancer cases, we also calculated the percentage of radiologists who located the lesion correctly. Spearman correlation coefficient was used to explore the association between two radiologist groups. Data demonstrated a high correlation between Chinese and Australian radiologists in identifying cancer cases (r=0.839, p<0.0001), and locating lesions (r=0.802, p<0.0001), but no statistically significant relationship in identifying normal cases (r=0.236, p=0.142). However, between radiologists from two geographic regions of China, strong correlations were found in detecting cancer cases (r=0.686, p=0.0008), marking lesions (r=0.803, p<0.0001) and recognizing normal cases (r=0.562, p=0.0002). In conclusion, although Chinese and Australian radiologists may share the same difficulty in diagnosing and locating cancers, a difference in the challenge of identifying normal cases between them was shown. However, the performance by radiologists within China, although from different regions, remained consistent when reading high-density mammograms.

Ab#040 An octadentate DFOB analogue to improve ligand performance in 89Zr-ImmunoPET imaging.

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Immunological positron emission tomography (immunoPET) imaging extends the potential of traditional positron emission tomography (PET), utilising immunological agents like monoclonal antibodies (mAbs) as targeting vectors. This improves the tumour-to-background ratio of images when compared to traditional PET images. Radiometal-based immunoPET imaging agents consist of a radionuclide, a ligand to coordinate the radiometal, and the targeting vector. 89Zr is an attractive choice as a radionuclide for immunoPET applications, possessing a half-life that closely matches the circulation time of mAbs. As 89Zr is a radiometal, an appropriate ligand is required to form a stable metal-ligand complex, preventing leaching of 89Zr and off-target pooling. Desferoxamine B (DFOB), a bacterial siderophore, exists as the current clinical choice of ligand for 89Zr-immunoPET applications. While DFOB has seen extensive clinical use as an Fe(III) chelator for secondary iron overload disease, it forms a suboptimal metal-ligand complex with 89Zr. 89Zr prefers octadentate coordination, with DFOB only able to offer hexadentate coordination through its 3 hydroxamic acid moieties. This leads to coordination of hydroxide/water ligands to saturate the coordination sphere of 89Zr, introducing instability to the metal-ligand complex. Previous studies have shown that introducing a fourth hydroxamic acid moiety to DFOB greatly improves the stability of the metal-ligand complex, however, current advances have struggled with hydrophilicity as a consequence of the additional hydroxamic acid. This work aims to generate a suitable ligand that incorporate a fourth hydroxamic acid moiety group into the DFOB scaffold while making additional chemical modifications to help retain or improve hydrophilicity when compared to DFOB and other tetrahydroxamic acid DFOB analogues. Improving the hydrophilicity and stability of the metal-complex is predicted to benefit the traction and uptake of Zr-89 in immunoPET and support its progression along the clinical pipeline.

Stream 2.4: Public health and cancer screening

Ab#042 Test-set training may increase breast screening cancer detection rates

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Mammographic test sets are a simulation-based training methodology for radiologists to assess and improve their performance. However, while test-set records have indicated over-time improvements in participants' performance within the tests, little is known about how those improvements translate into breast-screening readers' performance in the clinic. This study investigated how the performance of readers who completed test-set training in the BreastScreen Reader Assessment Strategy (BREAST) platform have evolved in comparison to readers who have no history of test-set participation. Investigating 10-year clinical audit data of 46 breast screening readers in New South Wales, Australia indicated that BREAST readers improved their positive predictive value (PPV) ($p=0.001$) in association with their test-set participation. They also had higher detection rates for invasive cancers ($p=0.01$), ductal carcinoma in situ (DCIS) ($p=0.03$), and the detection rate of all cancers and DCIS ($p=0.01$). In comparison, non-BREAST readers improved their recall rate in subsequent screens ($p=0.03$) and PPV ($p=0.02$). In conclusion, test-set participation is linked to enhanced capability of cancer detection, which can be due to the high proportion of cancer cases in the test sets in comparison to normal practice.

Keywords: screening mammography, breast cancer, mammographic test set, clinical audit, performance

Ab#043 Australian women's' intentions and psychological outcomes related to breast density notification and information: An online randomised experiment

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Aim: To quantitively assess how information provision of breast density information affects women's intention to undergo supplemental screening and to assess anxiety and breast cancer worry.
Methods: We conducted a three-arm online randomised experiment with Australian women (outside of Western Australia (WA)) aged between 40 and 74 years and with no prior history of breast malignancy. Women were randomised to receive control information (screening mammogram result without the breast density messaging) or one of two versions of the intervention (existing WA letter or health literacy sensitive letter) with breast density information included with the screen result letter.

Results: 1497 women were randomised. Compared to women who received screening mammogram result without the breast density messaging (n=518), significantly higher proportion of women who received breast density notification (n=501 and n=476) reported intention to seek supplemental screening (ultrasound or MRI) (2.5% versus 17.3% and 16.4%), undergoing screening mammogram more frequently (13.9% versus 27.1% and 25.6%), being anxious (14.7% versus 48.5% and 48.6%), feeling confused (8.1% versus 23.6% and 23.8%) , feeling quite or very worried about cancer (7.3% versus 17.4% and 15.6%) and intention to speak with a doctor (?to discuss further screening options??) (29.0% versus 67.5% and 65.9%). There were no (statistical??) differences in these outcomes between the two intervention groups. Nearly half of the women who received either of the intervention letters reported intention to do nothing differently and continue to have biennial screening mammogram (47.6% versus 48.5%). Compared to women who received the WA letter, significantly higher proportion of women who received the health literacy sensitive letter correctly answered questions about how common it is for women to have dense breasts (41.9% versus 57.3%) and the increased breast cancer risk (20.2% versus 58.3%); and significantly lower proportion of them correctly answered questions related to masking effect (80.0% versus 71.4%) and density decrease with age (61.3% versus 48.4%).

Conclusion: Breast density information/notification integrated with screening mammogram results likely to increase women's intention to undergo supplemental screening or more frequent mammography, and also potentially make women more anxious, confused, or worried. These findings have important implications for policy makers in considering the impacts of potential widespread notification of breast density.

Ab#044 General practitioner's attitudes and behaviours regarding cancer screening in older adults: A qualitative study

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Background: Many older adults continue to be screened for cancer with limited knowledge of the potential hams. General practitioners (GPs) likely play an important role in decision-making around cancer screening for older people.

Objective: To investigate GP's attitudes and behaviours regarding cancer screening (breast, cervical, prostate and bowel) in patients aged ≥70 years (given that national breast/cervical screening programs only recently extended to target women aged 70-74).

Method: Semi-structured interviews were conducted with GPs practising in Australia (n=27). Participants were recruited through multiple avenues to ensure variation in experience and geographic location (e.g., GP networks, social media, cold calling/emailing). Transcribed audio-recordings were analysed thematically.

Results: Some GPs only initiated screening discussions with patients younger than what they understood to be the upper targeted age of screening programs (i.e., 69 or 74 years). Others initiated discussions beyond recommended ages. When providing information, some GPs believed patients would need to pay to access screening, some were uncomfortable discussing why screening reminders stop, and detailed benefit and harms discussions were more likely for prostate screening. GPs described patients who were obliging, insistent on continuing/stopping, and those who were offended they were not invited anymore. When navigating patient-initiated discussions, GPs tailored their response to why the older person desired the screening test, but ultimately the patient had the final say. GPs considered the patient's overall health/function, risk, previous screening experience, and the reassurance needed as factors in whether screening was worthwhile in older age.

Conclusion: There is no uniform approach to cancer screening communication and decision-making for older adults in general practice. Given the role of patient preference, tools to support effective communication of the reduced benefit and increased chance of harm from cancer screening in older age may help support older people to make more informed screening choices.

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