THE UNIVERSITY OF SYDNEY

Sydney Cancer Conference 2021

SYDNEY CANCER CONFERENCE 2021

9-10 September

Program and Abstract Booklet

Contents

Welcome from the Sydney Cancer Conference 2021 Chairs

On behalf of the Sydney Cancer Conference 2021 (SCC2021) Organising Committee, we are pleased to welcome all delegates and speakers, as well as affiliate and sponsor partners, to this year's scientific meeting, which is proudly hosted by The University of Sydney. The appearance of COVID-19 has resulted in a three-year stretch since our last Sydney Cancer Conference. While current restrictions preclude us from physically getting together, our virtual meeting has given us the opportunity for global engagement; to educate, collaborate and share our knowledge and ideas. We are proud to present a world leading scientific program covering immunotherapy, novel drugs, biomarkers, cutting-edge imaging/radiology, psycho-oncology and the patient experience. We thank our fine array of speakers presenting under these themes over the course of the two days.

We were thrilled that SCC2021 was awarded "Consumers Included" status and to have consumer representatives contribute as valuable members of the organising committee; they certainly have helped to bring an important consumer perspective to the conference. We thank our affiliated organisations and sponsors for generously supporting the SCC meeting. Without their support, our SCC meeting would not be held. We encourage all delegates to support our partners, and drop by their virtual booths during the breaks throughout the program.

Thank you to everyone for attending this year's meeting, your support validates the time and effort that our volunteer committees put into organising such meetings. We trust you enjoy the meeting.

Kimberley Docking and Helen McGuire – Co-Chairs of SCC2021 Organising Committee

PROGRAM AT-A-GLANCE

Sydney Cancer Conference 2021

TIME	STREAM 1	STREAM 2	STREAM 3	POSTERS AND EXHIBITION ON-DEMAND
Session 1	**Opening Ceremony and Plenary** Chairs: *Dr Kimberley Docking and Dr Helen McGuire*			Sponsor exhibition + Mini-orals (Posters) available online on demand
9:30 am	Delegates log in, familiarise selves with platform and view virtual exhibition and virtual posters			
9:45 am	**Dr Kimberley Docking and Dr Helen McGuire,** SCC2021 Co-Chairs Welcome and housekeeping			
10:00 am	**Uncle Allen Madden - Welcome to Country**			
	Professor Robyn Ward AM, Executive Dean of the Faculty of Medicine and Health, The University of Sydney			
	Porfessor Mark Scott AO, Vice-Chancellor and Principal, The University of Sydney			
	The Hon Bronnie Taylor, MLC, Minister for Mental Health, Regional Youth and Women			
	Dr Kimberley Docking and Dr Helen McGuire SCC2021 Co-Chairs			
10:27 am	**Prof Theresa Whiteside** Professor of Pathology, Immunology and Otolaryngology, University of Pittsburgh School of Medicine; Member, UPMC Hillman Cancer Center, Pittsburgh, USA **Tumor-derived exosomes: their role in immune regulation and as biomarkers of cancer progression**			
11:02 am	**Prof Richard Scolyer** Conjoint Professor, The University of Sydney, FMH Translational Research Collective; Co-Medical Director Melanoma Institute Australia and Senior Staff Specialist at The Royal Prince Alfred Hospital & NSW Health Pathology. **Zero Deaths from Melanoma: Progress To Date and Prospects for the Future**			
11:37 am	**Short Break (15 min)**			
	Session 2 is proudly sponsored by		CIVICA	
Session 2 *Chairs*	**Omics** *Prof Rosemary Balleine, Dr Laveniya Satgunaseelan*	**Social determinants of cancer** *Prof Anne Cust, Dr Amy Vassallo*	**Precision medicine I** *Dr Justin Wong, Dr Sumit Sahni*	
11:52 am	sponsor message	sponsor message	sponsor message	
11:53 am	**A/Prof Mark Cowley** Children's Cancer Institute; ACRF and UNSW Medicine	**Dr Emma Webster** Rural Health, FMH, The University of Sydney **Who is the gardener? Racism as a social determinant of health**	**Prof Matt Dun** University of Newcastle and HMRI **Pharmcoproteogenomics for the development of combinatorial treatment regimens for paediatric high-grade gliomas.**	
12:13 pm	**Dr Ali Azimi** FMH Westmead Clinical School, The University of Sydney **Investigating Proteome Changes Between Primary and Metastatic Cutaneous Squamous Cell Carcinoma Using Mass Spectrometry**	**Ms Merran Findlay** RPAH and Chris O'Brien Lifehouse	**A/Prof Alexander Swarbrick** Garvan Institute of Medical Research **Exploring solid cancer ecosystems with cellular genomics**	
12:33 pm	**Dr Camelia Quek** 96: Identifying and targeting novel immunosuppressive driver mechanisms in young melanoma patients	**Dr Elvin Cheng** 107: Female hormonal factors and lung cancer death in never-smokers: results from China Kadoorie Biobank	**Dr Angela Ferguson** 118: High-dimensional and spatial analysis reveals immune landscape dependent progression in carcinoma	Designated exhibitor meeting time
12:48 pm	**Mr Lionel Leck** 146: Targeting Mitochondrial Dynamics to Prevent Drug Induced Cancer Stem Cells & MDR in Glioblastoma	**Dr Jie-Bin Lew** 25: Tailored colorectal cancer screening for Aboriginal and Torres Strait Islander peoples	**Dr Liz Caldon** 115: Endocrine therapy reprogramming of breast cancer leads to metastatic recurrence via Rac signalling	
1:03 pm	**Dr Julia Steinberg** 33: Genomic testing to identify CRC patients with Lynch syndrome: current practice and gaps in Australia	**Dr Deanne Jenkin** 112: Australian multiple myeloma incidence and mortality trends from 1982-2016 and projections to 2040	**Dr Caroline Atkinson** 122: Elevated P-glycoprotein confers resistance to multiple chemotherapies in high-risk neuroblastoma	
1:18 pm	**Dr Nicholas Nikesitch** 158: CMA mediates the ARPI stress response in prostate cancer, promoting ARPI treatment resistance	**Ms Nuray Yasemin Ozturk** 81: Knowledge and screening practices of cervical cancer among migrant women living in Sydney, Australia	**Dr Benjamin Heng** 78: Aggressive breast cancer subtype eats tryptophan!	
1:33 pm	**Prof Anna DeFazio** The University of Sydney and WIMR	**Prof Karen Canfell** The Daffodil Centre and FMH, The University of Sydney	**Prof Roger Reddel** The University of Sydney; CMRI; CellBank Australia, ProCan® **Integrating proteomic data into cancer precision medicine.**	Sponsor exhibition + Mini-orals (Posters) available online on demand
1:53 pm	**Short Break (15 min)**			Designated exhibitor meeting time
Session 3 **Chairs**	**PLENARY - PRECISION MEDICINE** *Prof Tim Shaw, Dr Dianne Sylvester*		abcam	
2:08 pm	sponsor message			
2:09 pm	**Dr Stephen Friend** Visiting Professor of Connected Medicine-University of Oxford, President/Founder- 4YouandMe, Chairman CoFounder of Sage Bionetworks **Precision Medicine from Genomics to use of Wearables to detect individual symptom trajectories**			
2:44 pm	**Prof David Thomas** Head, Genomic Cancer Medicine; Garvan Institute of Medical Research; Director, The Kinghorn Cancer Centre; Chief Executive Officer, Omico: Australian Genomic Cancer Medicine Centre; Conjoint Professor, St Vincent's Clinical School, Faculty of Medicine, UNSW **Precision medicine: from targeted therapies to management of cancer risk**			
3:19 pm	**PANEL: NSW Cancer Strategy 2021 and beyond** **Professor Anna DeFazio,** Chair, the Cancer Research Network and Sydney Cancer Partners **Dr Emma Heeley**, Manager, Grants & Data Intelligence, Strategic Research Investment, Cancer Institute NSW **Professor Don Nutbeam,** Executive Director, Sydney Health Partners **Professor Karen Canfell,** Director, The Daffodil Centre			Sponsor exhibition + Mini-orals (Posters) available online on demand
3:59 pm	**Short Break (15 minutes)**			
Session 4	**RESEARCH FUNDING WORKSHOP** *Dr Helen Mcguire*			
4:14 pm				
4:15 pm	**Professor Julie Redfern and Professor Ollie Jay,** Research Academic Directors (Researcher Development, Output and Impact), Faculty of Medicine and Health			
	Professor Anne Cust, Deputy Director, The Daffodil Centre, The University of Sydney, a joint venture with Cancer Council NSW; Melanoma Institute Australia; The University of Sydney			
	Dr David Waddington, ACRF Image X Institute, Sydney School of Health Sciences			
	Ms Fiona Pearson, Research Support Manager, Faculty of Medicine and Health			
4.30 pm	Q&A panle forum			
5:15 pm	**Break until evening session**			Opportunity to speak with poster presenters (1 hr, 5:15-6:15 pm)

PROGRAM AT-A-GLANCE

Sydney Cancer Conference 2021

Thursday 9 September 2021 - Evening Sessions				
	The Evening Clinical Sessions are proudly sponsored by: Merck Pfizer			
Session 5 *Chairs*	**Evening clinical session I** *Prof Michael Boyer, Prof Alexander Engel*	**Evening clinical session II** *Prof Geraldine O'Niell, Prof Stan Sidhu*		Sponsor exhibition + Mini-orals (Posters) available online on demand
7:00 pm	Introduction	Introduction		
7:04	**Message from Sponsor: Merck Healthcare**			
7:06 pm	**Dr Tracy King** Cancer Nursing Research Unit, The University of Sydney **Wombats and Devils: Measuring the impact of corticosteroids in those with multiple myeloma**	**Dr David Chan** Kolling Institute **Can PET scans replace biopsies for neuroendocrine tumours?**		
7:26 pm	**Dr Anupriya Agarwal** NHMRC Clinical Trials Centre, The University of Sydney **Title of talk: Let's talk money: How can we navigate the costs of cancer?**	**Prof Patrick Schlegel** WIMR, The University of Sydney		
7:46 pm	**Dr Geeta Sandhu** Cancer Institute NSW **Getting the dose right – Development of the International Consensus Guideline on Anticancer Drug Dosing in Kidney Dysfunction**	**Prof Jacob George** WIMR, Westmead Hospital and The University of Sydney **The future burden of primary liver cancer: MAFLD**		
8:06 pm	**Dr Kimberley Docking** School of Health Sciences, The University of Sydney **New National Clinical Practice Guidelines to Improve Speech, Communication & Swallowing in Children with Cancer**	**Dr Ines Silva** MIA, Westmead, Blacktown Hospitals,The University of Sydney **Challenges in the era of immunotherapy**		
8:26 pm	**Prof Jonathan Clark** Chris O'Brien Lifehouse	**A/Prof Angela Chou** Kolling Institute **A novel postneoadjuvant regression grading system predicts outcome in patient with resected pancreatic cancer**		
8:46 pm	**Dr Luciano Dalla-Pozza** The Children's Hospital at Westmead	**A/Prof Emily Blyth** Westmead Hospital and WIMR, The University of Sydney **Advanced cell therapies for safer and more effective stem cell transplant**		
9:06 pm	**End of clincial session and day**			

PROGRAM AT-A-GLANCE

Sydney Cancer Conference 2021

TIME	Stream 1	Stream 2	Stream 3	POSTERS AND EXHIBITION ON-DEMAND
	Friday 10 September 2021			
9:00 am	Opportunity to speak with poster presenters (1 hr, 9 - 10 am)			
Session 6 *Chairs*	**PATIENT EXPERIENCE & SOCIAL JUSTICE** *A/Prof Haryana Dhillon*		CIVICA	Sponsor exhibition + Mini-orals (Posters) available online on demand
10:00 am	sponsor message			
10:01 am	**Prof Ethan Basch** NC Cancer Hospital; UNC Gillings School of Global Public Health; Lineberger Comprehensive Cancer Center, The University of North Carolina, USA **Symptom Monitoring with Electronic Patient-Reported Outcomes in Cancer Care**			
10:36 am	**Prof Fran Baum** Southgate Institute for Health, Society and Equity, College of Medicine and Public Health, Flinders University			
11:06 am	**PANEL: Social Justice in Cancer Care** Facilitated by **A/Prof Haryana Dhillon**, School of Psychology, The University of Sydney **Prof Fran Baum** - Southgate Institute for Health, Society and Equity, College of Medicine and Public Health, Flinders University **Prof Alex Broom** - Sydney Centre for Healthy Societies, Faculty of Arts and Social Sciences, The University of Sydney **A/Prof Kelvin Kong** - MQ, UNSW, UoN, HMRI, Menzies School of Health Research, John Hunter Hospital, John Hunter Children's Hospital, and Hunter ENT **Prof Karen Canfell** - The Daffodil Centre, FMH, The University of Sydney **A/Prof Lisa Whop** - National Centre for Epidemiology and Population Health, ANU			Designated Exhibitor meeting time
12:06 pm	Break (15 minutes) - Lunch / exhibition / posters			
Session 7 *Chairs*	**CONSUMER FOCUS** *Ms Kathryn Leaney and Mr Murray McLachlan, Cancer Voices NSW*			
12:20 pm				
12:21 pm	**Ms Kathryn Leaney** Cancer Voices NSW **Consumers shaping research**			
12:41 pm	**PANEL: Cancer Consumers in Research** Facilitated by **Ms Kathryn Leaney and Mr Murray McLachlan,** Cancer Voices NSW **Mr Tony Maxwell -** Cancer survivor and consumer reviewer + **Prof Lisa Horvath** - Chris O'Brien Lifehouse; Central Clinical School, The University of Sydney; The Kinghorn Cancer Centre **Ms Lillian Leigh** - Cancer Australia and Thoracic Oncology Group of Australasia + **A/Prof Nick Pavlakis** - The University of Sydney; The Thoracic Oncology Group of Australasia; Genesis Care and RNSH **A/Prof Lynette Riley** - Sydney School of Education and Social Work,Indigenous Studies and Aboriginal Education, The University of Sydney + **Ms Karen Littlejohn** - The Foundation for Breast Cancer Care			Sponsor exhibition + Mini-orals (Posters) available online on demand
1:26 pm	Short break (15 minutes)			
	Session 8 is proudly sponsored by		abcam	
Session 8	**Drug development and new technologies** *A/Prof Kellie Charles, A/Prof Thomas Grewal*	**Supportive care & patient experience** *Prof Kate White, Ms Jingjing He*	**Cancer immunology** *Prof Georgina Clarke, Prof Mark Gorrell*	
1:41 pm	Sponsor message	Sponsor message	Sponsor message	
1:42 pm	**Dr Tristan Rawling** Mathematical and Physical Sciences, UTS **Targeting the proton gradient across the mitochondrial inner membrane for anticancer drug development**	**Dr Jasmine Yee** Exercise and Sport Sciences, The University of Sydney	**Dr Kavitha Gowrishankar** WIMR **T cell therapies- using native, chimeric and transgenic receptors**	
2:02 pm	**Dr Bekesho Geleta** 45: Targeting NDRG1 to inhibit bi-directional oncogenic cross-talk between pancreatic cancer and stroma	**Ms Lauren Ha** 39: Improving physical activity levels among childhood cancer survivors: A digital educational program	**Dr Kazi Nahar** 20: Systemic myeloid cells and local T cells propel immunotherapy-induced colitis	
2:17 pm	**Mr Josef Gillson** 90: Overcoming the chemoresistance mechanisms in pancreatic cancer via targeting the AMPK energy pathway	**Dr Rebecca Venchiarutti** 66: Health literacy and cancer care coordination among patients with head and neck cancer	**Miss Tiffany Tang** 38: Patient-derived xenograft (PDX) mouse models to test novel cell therapies for leukemia	
2:33 pm	**Dr Lin Xiao** 71: Targeting chromatin potently inhibits leukaemia progression in MLL-	**Ms Dorothy Drabarek** 153: Patient experiences of melanoma self-surveillance using mobile	**Dr Mawar Karsa** 34: CBL0137 promotes CART-cell therapy against MLL-rearranged	
2:47 pm	Short break (15 minutes)			
Session 9 *Chairs*	**Precision Medicine II** *Dr Camelia Quek , Dr Leonard Goldstein*	**Psycho-Oncology** *A/Prof Jo Shaw, Dr Carolyn Mazariego-Jones*	**Medical Radiation Sciences** *Prof Dale Bailey, Dr Ernest Ekpo*	
3:02 pm				
3:03 pm	**Dr Emily Colvin** Kolling Institute and The University of Sydney **The role of lncRNAs in the ovarian tumour microenvironment**	**Rachel Campbell** Quality of Life Office, The University of Sydney **Measuring what matters MOST in ovarian cancer clinical trials and clinical practice.**	**Prof Patrick Brennan** Medical Radiation Sciences, The University of Sydney, DetectED-X **Multiple academic outputs from a simple educational initiative**	
3:23 pm	**Prof Jean Yang** The Universtiy of Sydney **Harnessing single-cell data for cancer**	**Prof Phyllis Butow** PoCoG & CeMPED, School of Psychology; SoURCe, Institute of Surgery, The University of Sydney **A clinical pathway for anxiety and depression (ADAPT) in the cancer setting: Implementation outcomes.**	**Prof Annette Haworth** Medical Physics, Faculty of Science, The University of Sydney **Biologically Targeted Radiotherapy: utilising imaging biomarkers to characterise tumour heterogeneity for precision radiation therapy**	
3:43 pm	**Dr Robert Finnegan** 99: A Three-Dimensional Computational Model of Prostate Cancer Biology	**Ms Sarah Ratcliffe** 126: Moral distress among oncology and palliative care HCPs in Australia: A qualitative study.	**Dr Caterina Brighi** 15: Stability of multiparametric MR imaging biomarker-derived dose prescriptions for glioblastoma	
3:58 pm	**Prof Mark Molloy** 100: Integrated Molecular Analysis of Polyps (IMAP) study to understand how bowel polyps develop	**Dr Jennifer Cohen** 36: Canteen Connect: The evaluation of an online health community for AYAs impacted by cancer	**Miss Faiqa Mudassar** 54: Investigating Novel Treatments to Improve Radiation Response in Diffuse Intrinsic Pontine Glioma	
Session 10 *Chairs*	**Closing remarks & awards presentation** *Dr Helen McGuire and Dr Kimberley Docking, SCC2021 Co-Chiars* *Professor Anna DeFazio, Conveynor, the Cancer Research Network, Faculty of Medicine and Health, University of Sydney*			Sponsor exhibition + Mini-orals (Posters) available online on demand
4:28 pm	Closing remarks & awards presentationDr Helen McGuire and Dr Kimberley Docking, SCC2021 Co-Chiars Professor Anna DeFazio, Conveynor, the Cancer Research Network, Faculty of Medicine and Health, University of Sydney			
5:00 pm	END OF CONFERENCE			

SCC2021 Speaker's Affiliations

ACRF - Australian Cancer Research Foundation
ANU - Australian National University
CeMPED - Centre for Medical Psychology & Evidence-Based Decision-Making
CMRI - Children's Medical Research Institute
FMH - Faculty of Medicine and Health (The University of Sydney)
HMRI - Hunter Medical Research Institute
MIA - Melanoma Institute Australia
MQ - Macquarie University
PoCOG - Psycho-Oncology Co-operative Research Group
RNSH - Royal North Shore Hospital
SOuRCe - Surgical Outcomes Research Centre
UNSW - University of New South Wales
UoN - University of Newcastle
UTS - University of Technology Sydney
WIMR - Westmead Institute for Medical Research

COMMITTEE LISTS

ORGANISING COMMITTEE SCC2021

Dr Kimberley Docking, CoChair
Dr Helen McGuire, Co-Chair
Dr Cathy Barnett
Dr Marcel Batten
Ms Shirley Baxter
Dr Megan Best
Dr Rachel Campbell
Dr Ernest Ekpo
Prof Guy Eslick
Mr Michael Evtushenko
Ms Gai Grayson
Ms Jingjing He
Ms Merilyn Heuschkel
Dr Viive Howell
Ms Tiffany Li
Ms Rachel Love
Dr Carolyn Mazariego-Jones
Ms Cara McFarlane
Ms Suzie Ngyuen
Dr Camelia Quek
Ms Susie Redfern
Ms Bronwyn Robertson
Dr Sumit Sahni
Dr Laveniya Satgunaseelan
Dr Amy Vassallo

SCIENTIFIC ADVISORY

Prof Anna DeFazio (CRN Interim-Chair)
Prof Alexander Engel (Executive member)
Prof Roger Reddel (Executive member)
Prof Tim Shaw (Executive member)
Prof Dale Bailey
Prof Patrick Brennan
Prof Michael Boyer
A/Prof Kellie Charles
Prof Stephen Clarke
Dr Kristina Cook
A/Prof Teresa Davis
A/Prof Haryana Dhillon
Dr Rachael Dodd
Prof David Feng
Prof Trevor Hambley
Prof Paul Harnett
Dr Jolyn Hersch
Prof Mark Krockenberger
Prof Laurent Rivory
Prof Kate White
A/Prof Peter Williamson
Prof Jean Yang
Prof Jane Young
Prof Hans Zoellner

COMMITTEE LISTS

AFFILIATED ORGANISATIONS

The University of Sydney
The University of Sydney Cancer Research Network
Sydney Catalyst Translational Cancer Research Centre
Sydney West Translational Cancer Research Centre
Sydney Vital Translational Cancer Research Centre
Kids Cancer Alliance Translational Cancer Research Centre
Sydney Health Partners

COMMITTEE LISTS

PROGRAM COMMITTEE

Dr Anupriya Agarwal
Dr Mir Massoud Aghili Yajadda
Dr Ali Azimi
Miss Sarah Bae
Mr Jay Balante
Dr Hana Bali
Dr Marcel Batten
Ms Shirley Baxter
Prof Michael Boyer
Dr Kim Tam Bui
Dr Rachel Campbell
Dr Jinbiao Chen
Dr Karen Chiam
Dr Hassan Choucair
Dr Kristina Cook
Prof Anna DeFazio
Dr Kimberley Docking
Dr Rachael Dodd
Dr Ernest Ekpo
Prof Guy Eslick
Dr Robert Finnegan
Dr Yaser Hadi Gholalmi
Prof Mark Gorrell
Dr Kavi Gowrishankar
Ms Gai Grayson
A/Prof Thomas Grewal
Dr Susannah Hallal
Professor Trevor Hambley
Ms Jingjing He
Dr Elham Hosseini-Beheshti
Dr Anna Janssen
Dr Deanne Jenkin
Dr Yobelli Jimenez
Dr Yoon-Jung Kang
Dr Sukriti Krishan
Mr Lionel Leck
Ms Tiffany Li
Miss Chloe Lim
Mrs Ann Livingstone
Dr Chenkai Ma
A/Prof Michele Madigan
Dr Carolyn Mazariego-Jones
Dr Helen McGuire
Dr Rebecca Mercieca-Bebber
Professor Mark Molloy
Mr Marco Mueller
Dr Visalini Nair-Shalliker
A/Prof Matt Naylor
Dr Sianne Oktaria
Dr Chiara Pantarelli
Dr Lara Petelin
Dr Kristen Pickles
Dr Camelia Quek
Professor Roger Reddel
Dr Sumit Sahni
Ms Nancy Santiappillai
Dr Peter Sarich
Dr Laveniya Satgunaseelan
Dr Naisana Seyedasli
Professor Stan Sidhu
Dr Mo'ayyad Suleiman
Dr Dianne Sylvester
Dr Sirisha Tadimalla
Dr Pegah Varamini
Dr Amy Vassallo
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Dr Marianne Weber
Prof Kate White
Ms Sarsha Yap
Dr Razia Zakarya

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Sydney Cancer Conference 2021

INVITED SPEAKER BIOGRAPHIES

INVITED SPEAKERS

List by session

1. OPENING CEREMONY & PLENARY

Uncle Allen Madden
Professor Robyn Ward AM
Professor Mark Scott AO
The Hon. (Bronnie) Bronwyn Taylor, MLC
Professor Theresa Whiteside
Professor Richard Scolyer AO

2A. Omics

Associate Professor Mark Cowley
Dr Ali Azimi
Professor Anna DeFazio

2B. Social determinants of cancer

Professor Karen Canfell
Ms Merran Findlay
Dr Emma Webster

2C. Precision medicine I

Associate Professor Matt Dun
Professor Roger Reddel AO
Associate Professor Alexander Swarbrick

3. PLENARY: PRECISION MEDICINE

Dr Stephen Friend
Professor David Thomas

5A. Clinical I

Dr Anupriya Agarwal
Professor Jonathan Clark AM
Dr Kimberley Docking
Dr Tracy King
Dr Geeta Sandhu
Dr Luciano Dalla Pozza

5B. Clinical II

Associate Professor Emily Blyth
Dr David Chan
Associate Professor Angela Chou
Professor Jacob George
Professor Patrick Schlegel
Dr Ines Silva

INVITED SPEAKERS

List by session

6. PLENARY: PATIENT EXPERIENCE & SOCIAL JUSTICE

Professor Ethan Basch
Professor Fran Baum AO

(6) PANEL: SOCIAL JUSTICE IN CANCER CARE

Associate Professor Haryana Dhillon – *Facilitator*
Associate Professor Lisa Whop
Professor Karen Canfell
Professor Alex Broom
Professor Kelvin Kong

7. PLENARY: Consumer focus

Ms Kathryn Leaney - *Plenary speaker, session co-chair and panel co-facilitator*

(7) PANEL: SUCCESSFUL CONSUMER-RESEARCHER COLLABORATION

Mr Murray McLachlan - *Co-facilitator and session co-chair*
Professor Lisa Horvath
Ms Lillian Leigh
Karen Littlejohn
Mr Tony Maxwell
Associate Professor Nick Pavlakis
Associate Professor Lynnette Riley

8A. Drug development and new technologies

Dr Tristan Rawling

8B. Supportive care and patient experience

Dr Jasmine Yee

8C. Cancer immunology

Dr Kavitha Gowrishankar

9A. Precision medicine II

Dr Emily Colvin
Professor Jean Yang

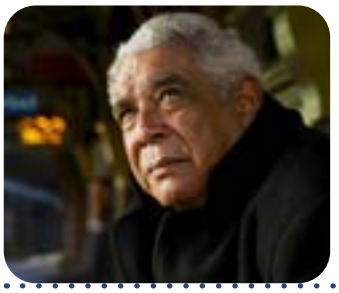
9B. Psycho-Oncology

Professor Phyllis Butow AM
Dr Rachel Campbell

9C. Medical Radiation Oncology

Professor Patrick Brennan
Professor Annette Haworth

1. OPENING CEREMONY & PLENARY



Uncle Allen Madden

Gadigal Elder

Uncle Allen John Madden was born in 1949 in Redfern. He has worked for Sydney City Council, Aboriginal Medical Service, Aboriginal Children's Service, Aboriginal Legal Service, NCAP and New Careers for Aboriginal People Employment. Uncle Madden has been on the board of Sydney Foreshore Authority, the Central Coast Aboriginal Heritage and many others and is a board member of the MLALC. He is a married man with 10 children, a Gadigal Elder and Business owner of Aboriginal Land Consultancy which promotes WTC, Site Surveys and Aboriginal Tours.

Professor Mark Scott AO

Vice-Chancellor and Principal, The University of Sydney

Professor Mark Scott was appointed as the University's 27th Vice-Chancellor in 2021. He is a highly respected and successful senior leader of large and complex institutions, across public service, education and the media.

The Hon. Bronwyn (Bronnie) Taylor

Member of the Legislative Council, Minister for Mental Health, Regional Youth and Women, Member of The Nationals

Minister Taylor is passionately committed to our rural and regional communities, and in particular about health and education outcomes, local government and agriculture. For 20 years prior to her election, Minister Taylor was a registered nurse, specialising in cancer care and palliative care. Her work in these fields saw her become one of the first McGrath Foundation Breast Care nurses, and then she went on to become the Director of Cancer Services in the Southern NSW Local Health District.

1. OPENING CEREMONY & PLENARY

Dr Theresa Whiteside

Professor of Pathology, Immunology and Otolaryngology, University of Pittsburgh School of Medicine; Member, UPMC Hillman Cancer Center, Pittsburgh, USA

Dr Whiteside received both her MA and PhD degrees in Microbiology from Columbia University, New York, NY. She is a Diplomate of the American Board of Medical Laboratory Immunology (1979). She was a Fogarty Senior International Fellow at the Ludwig Institute for Cancer Research in Lausanne, Switzerland (1984-85). At the University of Pittsburgh, Dr Whiteside rose through the faculty ranks to become Professor of Pathology with secondary appointments as Professor of Immunology and Otolaryngology (1989-present). She served as Director of the Immunologic Monitoring and Cellular Products Laboratory (IMCPL) at the UPMC Hillman Cancer Center for 25 years and is now its Interim Director. Dr Whiteside's research has been focused on mechanisms of tumor-induced immunosuppression, cytokine networks, development of anticancer vaccines, immunobiology of human tumors and the role of natural immunity in the control of cancer progression. She studies mechanisms of tumor escape from the host immune system and the development of therapies designed to eliminate tumor escape. Most recently, she has been investigating tumor-derived exosomes (TEX) and their role in cancer-induced immune suppression. She has authored 615 peer-reviewed papers and 175 chapters and review articles. She received a Honoris causa degree in Medicine from The Poznan Medical University in Poland in 2011 and was awarded a Richard V. Smalley Memorial Award by the Society of Immunotherapy of Cancer in 2012.

Professor Richard Scolyer AO

Conjoint Professor, The University of Sydney, FMH Translational Research Collective; Co-Medical Director Melanoma Institute Australia and Senior Staff Specialist at The Royal Prince Alfred Hospital & NSW Health Pathology

Professor Richard Scolyer BMedSci, MBBS, MD, FRCPA, FRCPath, FAHMS is Senior Staff Specialist, Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital; Co- Medical Director, Melanoma Institute Australia; and Conjoint Professor, Faculty of Medicine and Health, The University of Sydney. He provides a clinical consultation service for the diagnosis of difficult pigmented lesions and receives more 2000 cases for opinion from Australasia and beyond annually. He effectively integrates his clinical practice with leading an award-winning translational melanoma research laboratory. His record includes co-authoring more than 700 peer reviewed publications and/or book-chapters with >45,000 citations and a h-index of 107.

1. OPENING CEREMONY & PLENARY

Professor Robyn Ward AM FAHM

Executive Dean and Pro Vice-Chancellor Medicine and Health, Faculty of Medicine and Health, The University of Sydney

Professor Ward joined the University of Sydney in July 2018 as the inaugural Executive Dean of the Faculty of Medicine and Health. She was the former Deputy Vice-Chancellor (Research) and Executive Dean (Acting) of the Faculty of Medicine of the University of Queensland.
Professor Ward is an academic leader, cancer researcher and medical oncologist. She is a member of the Pharmaceutical Benefits Advisory Committee (PBAC), chairs the Commonwealth Medical Services Advisory Committee (MSAC), and serves on the Council and Executive of the Australian Academy of Health and Medical Sciences. In 2013 she was made Member of the Order of Australia (AM) for significant service to medical research and patient care in the field of oncology.

2A. Omics

Associate Professor Mark Cowley

Group Leader, Computational Biology at Children's Cancer Institute; Co-head of the Luminesce Alliance Childhood Cancer Computational Biology Program; Co-head of the ACRF Child Cancer Liquid Biopsy Program; Conjoint Associate Professor with the School of Women's and Children's Health, UNSW Medicine

Associate Professor Mark Cowley is a computational biologist, whose expertise is in genomics and precision medicine. Mark's group develops novel approaches to understand the molecular basis of disease. His team also develops the digital infrastructure that underpins the Zero Childhood Cancer Program, an ambitious national research program that uses precision medicine to diagnose and treat Australian children with cancer. Mark is now also the co-head of the ACRF Childhood Cancer Liquid Biopsy program, a program aiming to improve health outcomes by developing sensitive new approaches to monitor patients over time.

Dr Ali Azimi

Research Associate, Westmead Clinical School, Faculty of Medicine and Health, The University of Sydney

Dr Azimi received his PhD in non-melanoma skin cancer proteomics from the University of Sydney in 2019. He is now a Post-doctoral Cancer Research Associate with the Westmead Clinical School, Faculty of Medicine and Health, the University Sydney. His primary research interest is next generation proteomic workflows that impact skin lesion diagnosis, classification and intervention. He was awarded the Sydney West Transitional Cancer Research (SW-TCRC) Fellowship in 2019 and the SW-TCRC Early Career Accelerator Grant in 2020. Dr Azimi collaborates closely with clinicians at Westmead and Royal Prince Alfred hospitals, and is interested to develop a novel tape-stripping approach for non-invasive diagnosis of skin cancers that would otherwise need invasive surgical interventions.

2A. Omics

Professor 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

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.

2B. Social determinants of cancer

Professor Karen Canfell

Director, The Daffodil Centre; Professor & NHMRC Leadership Fellow, Faculty of Medicine and Health, The University of Sydney

Professor Karen Canfell is the inaugural Director of the Daffodil Centre, a joint venture between the University of Sydney and Cancer Council NSW. She is an epidemiologist, modeller, and a translationally-focused population health researcher. She has led evaluations of new cancer screening approaches for government agencies in several countries. She currently leads Compass, which is the first major international experience of cervical screening in an HPV-vaccinated population. Her team's work underpins the 2017 transition of the National Cervical Screening Program in Australia from Pap smears to 5-yearly HPV-based screening. She currently has active collaborative modelling grants from the US NIH and WHO to model cervical cancer prevention in the USA and globally. Her work as one of the co-leads of the WHO Cervical Cancer Elimination Modelling Consortium was presented and discussed at the Executive Board of the World Health Assembly in 2020 and supported the formal resolution by WHO to support the cervical cancer elimination initiative, launched in late 2020.

Ms Merran Findlay

Executive Research Lead, Cancer Nutrition at Royal Prince Alfred Hospital, Sydney Local Health District

Ms Findlay is the Executive Research Lead-Cancer Nutrition at Royal Prince Alfred Hospital, Sydney Local Health District working in partnership with Chris O'Brien Lifehouse where she holds an appointment as Oncology Dietetics Clinical Research Fellow. Specialising in nutrition support of people with cancer for more than 20 years, she is recognised as an Advanced Accredited Practising Dietitian and currently serves as Chair of the national Clinical Oncology Society of Australia (COSA) Nutrition Group. Ms Findlay is a recent National Health and Medical Research Council Translating Research Into Practice Fellow and current Sydney Research PhD Scholar. Her research interests include the impact of skeletal muscle status, nutritional status and nutrition intervention on clinical, cost and patientcentred outcomes as well as evidence synthesis, dissemination and implementation. As Adjunct Senior Lecturer, she actively contributes to the cancer nutrition teaching program in the Faculty of Medicine and Health at the University of Sydney.

2B. Social determinants of cancer

Dr Emma Webster

Senior Lecturer Rural Research, School of Rural Health, Faculty of Medicine and Health, The University of Sydney

Dr Webster is a Senior Lecturer in Rural Research at the University of Sydney, School of Rural Health based in Dubbo in western NSW. She is recognised for her pragmatic and collaborative approach to research and her genuine desire to engage academia to serve community interests. She has experience applying decolonising approaches to enhance participation of Aboriginal people in research design and conduct. She also has an interest in exploring bicultural models of care which give proper recognition to the value of Aboriginal cultural protocols and practices in healthcare. Having supervised over 100 novice researchers to undertake their first research project, Dr Webster is passionate about supporting rural clinicians to enhance their research skills and helping rural organisations build their capacity for research.

2C. Precision medicine I

Associate Professor Matt Dun

Associate Professor, The University of Newcastle (UON) Faculty of Health & Medicine, Hunter Medical Research Institute (HMRI)

Associate Professor Matt Dun received his PhD from the University of Newcastle in 2012. He has been decorated by >25 national and international awards, including the 2019 NSW Premier's Awards for Outstanding Cancer Research Fellow and a Young Tall Poppy Award in 2020. Associate Professor Dun has secured successive Cancer Institute NSW Early Career Fellowships (2014-2016 and 2017-2019), an NHMRC Investigator Grant (2020-2025), a Defeat DIPG Chadtough New Investigator Grant (2020-2021) and successful Cancer Institute NSW and NHMRC Equipment Grants to establish a high-resolution mass spectrometry platform at the University of Newcastle. Associate Professor Dun guides the Cancer Signalling Research Group at the University of Newcastle and the Hunter Medical Research Institute, which focuses on paediatric leukaemia and brain cancer research. His group employs sophisticated pharmaco-phospho-proteo-genomics techniques to characterise the cellular signalling pathways dysregulated by the genetic individualities of a patient's cancer. This profiling strategy attempts to identify novel treatment targets and drug combinations to improve survival.

2C. Precision medicine I

Professor Roger Reddel AO

Sir Lorimer Dods Professor, Faculty of Medicine and Health, The University of Sydney; Director, Children's Medical Research Institute (CMRI); Co-Director of ProCan®.

Professor Roger Reddel is Director of Children's Medical Research Institute (CMRI) and Lorimer Dods Professor, Faculty of Medicine and Health, University of Sydney. His training included medical degrees from the University of Sydney, clinical training in medical oncology, a PhD in cancer cell biology, and postdoctoral research at the US National Cancer Institute. His research at CMRI investigates the unlimited replicative potential ("immortalization") of cancer cells. He and his team are known internationally for discoveries regarding the role of telomere length maintenance in immortalization, and especially the discovery of the Alternative Lengthening of Telomeres mechanism. He is also a co-founder of the ProCan program, which is focussed on delivery of proteogenomic data to the cancer clinic. A Fellow of the Australian Academy of Science and of the Australian Academy of Health and Medical Sciences, Professor Reddel has been awarded the Ramaciotti Medal, the NSW Premier's Award for Outstanding Cancer Researcher, and the Neil Hamilton Fairley Medal of the Royal Australasian College of Physicians.

Associate Professor Alexander Swarbrick

Principal Research Fellow & Laboratory Head, Garvan Institute of Medical Research; Associate Professor, St Vincent's Clinical School, Faculty Of Medicine, UNSW Sydney

Associate Professor Swarbrick is a Principal Research Fellow in the Garvan Institute of Medical Research; a conjoint associate professor at UNSW and an NHMRC Senior Research Fellow. Associate Professor Swarbrick completed his PhD at UNSW, followed by a postdoctoral fellowship with J. Michael Bishop at UCSF. His lab applies cellular genomics to human breast & prostate cancer & melanoma to gain systems-level insights into disease aetiology and the development of novel treatment strategies.

3. PLENARY: PRECISION MEDICINE

Dr Stephen Friend
Visiting Professor of Connected Medicine-University of Oxford, President/Founder- 4YouandMe, Chairman CoFounder- Sage Bionetworks

Dr Friend is an authority in the fields of genetic resilience, cancer biology, and digital health. At Dana Farber and MIT his team cloned the first human cancer susceptibility gene. While on the Faculty at Harvard, he was jointly recruited with Lee Hartwell to co-found "The Seattle Project" at the Hutch and then co-founded and led Rosetta Impharmatics were they developed the RNA expression approaches to assess the aggressiveness of breast cancers. Merck acquired Rosetta and as SVP for Oncology he rebuilt the cancer franchise using molecular profiling techniques, which would later show value in assessing the sensitivity of tumors to Keytruda. After working at Apple on Special Projects Team from 2014-2017, he is now a co-founder of 4YouandMe, the Founder and Chairman of Sage Bionetworks, and based Oxford as a Visiting Professor of Connected Medicine. Stephen is both an Ashoka fellow and a AAAS Fellow.

Professor David Thomas
Head, Genomic Cancer Medicine; Garvan Institute of Medical Research; Director, The Kinghorn Cancer Centre; Chief Executive Officer, Omico: Australian Genomic Cancer Medicine Centre; Conjoint Professor, St Vincent's Clinical School, Faculty of Medicine, UNSW

Professor David Thomas is the Director of The Kinghorn Cancer Centre and a NHMRC Principal Research Fellow at the Garvan Institute of Medical Research. As a clinician-scientist, his focus is on the application of genomic technologies to the understanding and management of cancer. Professor Thomas founded the Australasian Sarcoma Study Group, a national research organisation, and established Australia's leading adolescent and young adult cancer unit at the Peter MacCallum Cancer Centre. Professor Thomas leads the International Sarcoma Kindred Study, now recruiting from 23 centres in 7 countries, and led the first international study of denosumab in Giant Cell Tumor of bone, leading to FDA and TGA approval. He has over 200 research publications, including lead or senior author papers in Science, Cancer Cell, Molecular Cell, Journal of Clinical Investigation, Lancet Oncology, JAMA Oncology, and Journal of Clinical Oncology. Since moving to NSW, he has established the Australian Genomic Cancer Medicine Centre as well as Omico, a national precision medicine program for patients with rare and early onset cancers. In 2018, he was President of the Connective Tissue Oncology Society, the peak international body in his field.

5A. Clinical I

Dr Anupriya Agarwal
NHMRC Clinical Trials Centre, The University of Sydney

Dr Anupriya Agarwal is a medical oncologist and a PhD candidate at the University of Sydney. Her clinical practice is focused on breast and thoracic malignancy and other advanced cancers. Her PhD research interests focus on researching the effects of costs of cancer care on patients. Dr Agarwal is also invested in teaching and training as a Clinical Associate Lecturer and tutor at the University of Sydney. She is a member of the NSW Medical Oncology Advanced Trainee Committee and a Member of the Oncology Drugs Working Group with MOGA.

Professor Jonathan Clark AM
Director of Head and Neck Research, Lang Walker Family Foundation Chair in Head and Neck Cancer Reconstructive Surgery, Chris O'Brien Lifehouse; Sydney Medical School, Faculty of Medicine and Health, The University of Sydney; Royal Prince Alfred Institute of Academic Surgery

Professor Clark is a Head and Neck ablative and reconstructive surgeon at Chris O'Brien Lifehouse. He is the Lang Walker Family Foundation Professor and Chair in Head and Neck Cancer Reconstructive Surgery at the University of Sydney, Director of head and neck cancer research at Lifehouse, and Director of Translational Research at the Royal Prince Alfred Institute of Academic Surgery. Professor Clark undertook a two-year fellowship in Head and Neck oncologic and reconstructive surgery in, Toronto, Canada. Professor Clark's clinical expertise and research focus is in the areas of salivary gland tumours, oral cancer, digital planning for precision jaw reconstruction and dental rehabilitation, facial nerve reconstruction, advanced skin cancer, and transoral robotic surgery (TORS). He has trained > 30 international surgeons in microvascular reconstruction and has > 270 peer review publications. He is a Member of the Order of Australia (AM) for contributions to head and neck surgery and faculty in the International Federation of Head and Neck Oncological Societies (IFHNOS) Masters of Surgery.

5A. Clinical I

Dr Kimberley Docking

Sydney School of Health Sciences, Faculty of Medicine and Health, The University of Sydney

Dr Kimberley Docking is a Speech Pathologist and Director of the NeuroKids Communication Research Laboratory in the Faculty of Medicine and Health at The University of Sydney, which aims to improve the quality of life and communication of children surviving cancer and brain injury. Kimberley recently led development of world-first NHMRC-approved Clinical Practice Guidelines for the management of communication and swallowing disorders in children diagnosed with brain tumour and leukemia. She is Co-Chair of the Sydney Cancer Conference 2021.

Dr Tracy King

Myeloma Clinical Nurse Consultant, Royal Prince Alfred Hospital, NSW; Clinical Research Fellow and Clinical Lecturer, Cancer Nursing Research Unit, Faculty of Medicine and Health, The University of Sydney

Dr King is a Myeloma Clinical Nurse Consultant at Royal Prince Alfred Hospital; Clinical Research Fellow and Lecturer at the Cancer Nursing Research Unit, Sydney University. Dr King completed a master's in nursing leadership and was recently awarded her PhD with Sydney University. She was awarded the Outstanding Research Achievement Nursing & Midwifery Award 2019 by Sydney Local Health Network (SLHD) for her leadership and research in better understanding the experiences of those affected by myeloma taking high dose steroids and the role of patient reported outcome measures (PROM). With over 30 years' experience in the field of Haematology / BMT, Dr King developed a specialist interest in myeloma 20 years ago while working with the International Myeloma Foundation (IMF), now Myeloma UK. Since coming to Australia Dr King has been an active member of a range of national and international professional working groups including those of the Cancer Institute NSW; Myeloma and Related Disease Registry (MRDR), Chair of the HSANZ Myeloma Special Practice Network (M-SPN) and Past President and co-founder of the HSANZ Nurses Group. Most recently Dr King has been invited as a member of the IMF Nurse Leadership Board (NLB) and leads the nurse's program development and delivery during the International Myeloma Workshop (IMW).

5A. Clinical I

Dr Geeta Sandhu
eviQ Project Pharmacist, Cancer Institute New South Wales

Dr Geeta Sandhu graduated with a Bachelor of Pharmacy degree with First Class Honours in 2003. She went on to complete her Post-graduate Diploma in Clinical Pharmacy in 2007. She completed her Doctor of Philosophy at the University of Queensland in 2017, analysing the impact of increasing patient weight on the dosing of chemotherapy in lymphoma patients. Dr Sandhu has over 15 years of experience working in cancer care in various clinical roles in adult and paediatric care, medication safety and managing electronic prescribing systems for cancer. She is currently working on an international project for eviQ at the Cancer Institute NSW. Dr Sandhu has presented at multiple interdisciplinary cancer conferences and educational seminars in addition to involvement in university teaching for cancer care and pharmacometrics.

Dr Luciano Dalla Pozza
Director, Cancer Centre for Children; Senior Staff Specialist, The Children's Hospital at Westmead

Dr Luciano Dalla-Pozza is a member of key medical subspecialty societies whose mission is focused on the research and care of children and adolescents with cancer. His interest and recent work has centred on the management of acute leukaemia particularly the application of the new immunotherapies, the development of clinical trials and basic research opportunities in paediatric oncology, and the introduction of home based care for children with cancer. Dr Dalla-Pozza is a member of the NSW Child Death Review Team (NSW Ombudsman's Office), the Australasian Children's Clinical Trial group of ANZCHOG and the Executive of the Kids Cancer Alliance (NSW Cancer Institute). He is the Institutional Lead for The Therapeutic Advances in Childhood Leukaemia (TACL) Consortium and Principle Investigator at The Children's Hospital of the AEIOP-BFM 2017 trial for children with acute lymphoblastic leukaemia. He is Chair of Cancer Australia's Children's Cancer web-section group, he is the Clinical Lead for the Oncology Electronic Medical record at the Children's Hospital at Westmead and oversaw the introduction of the first fully electronic Oncology chemotherapy protocol ordering system in Australia (amongst the very first in the world). He chaired three Victorian Paediatric Integrated Cancer Services Steering Committees for the development of Clinical Pathways for children and adolescents with leukaemia, solid tumours and brain tumours.

5B. Clinical II

Associate Professor Emily Blyth

Senior Staff Specialist Haematologist, Clinical Lead, Immune Effector Cell Therapies, Westmead Hospital; NSW Cancer Institute Post-Doctoral Fellow, Westmead Institute for Medical Research, University of Sydney

Associate Professor Blyth is the Clinical Lead for Immune Effector Cells at Westmead Hospital in NSW. She is a haematologist, bone marrow transplant and cell therapy physician and a post-doctoral research fellow at the Westmead Institute for Medical Research at the University of Sydney. She has a clinical interest in transplant and cellular therapies. She is a Research Lead in the Westmead Cell Therapies Group's clinical trial program and a member of the Sydney Cell and Gene Therapy Strategic Committee which is focused on bringing cell and gene therapy technologies to patients in clinical trials at the Westmead Campus. Her research interests are in the use of cellular therapy to improve quality of life and survival in patients with blood cancers and those undergoing blood stem cell transplantation.

Dr David Chan

Bill Walsh Translational Cancer Research Laboratory, Kolling Institute, Northern Clinical School, University of Sydney

Dr David Chan is a clinician-researcher interested in neuroendocrine tumours (NETs). After completing his medical oncology training in Sydney, he spent two years in a research fellowship in Toronto, Canada before returning to complete his PhD on PET scans as biomarkers in NETs. He is the recipient of a NHMRC Emerging Leadership grant furthering this research, and is the chair of the NET group for the Clinical Oncology Society of Australia. He has published more than 60 peerreviewed articles (35 in the field of NETs). He is works part-time as a medical oncologist at Royal North Shore Hospital, and enjoys spending any time off with his wife and two kids.

5B. Clinical II

Associate Professor Angela Chou

Clinical Associate Professor, Northern Clinical School, University of Sydney; Senior Staff specialist, Department of Anatomical Pathology, Royal North Shore Hospital; Cancer Diagnosis and Research Group, Kolling Institute

Associate Professor Angela Chou is a surgical pathologist at Royal North Shore Hospital and a cancer researcher at the Kolling Institute. She graduated from Medicine at University of NSW and obtained her Fellowship from the Royal College of Pathologists in 2010. In 2017 she was awarded a PhD from the University of NSW for her research titled 'Novel therapeutic strategies for the treatment of pancreatic cancer.' Last year, Angela was awarded the Cancer Institute of NSW Early Career Cancer Research Fellow Award for her research in pancreatic cancer.

Professor Jacob George

Robert W Storr Chair of Hepatic Medicine, the University of Sydney; Director, Storr Liver Centre, The Westmead Institute for Medical Research; Head, Department of Gastroenterology & Hepatology, Westmead Hospital

Jacob George is the Robert W. Storr Professor of Hepatic Medicine at the Storr Liver Centre, Westmead Institute for Medical Research, University of Sydney and Head of the Department of Gastroenterology and Hepatology at Westmead Hospital. He undertakes basic and clinical research on liver cancer, MAFLD, hepatitis C, and hepatic fibrosis. He is an Associate Editor for the Journal of Hepatology, is a board member of the Gastroenterological Society of Australia and is current Chair of its Liver Faculty. He has published >500 papers, has >43,000 citations and an h index of 91. He was recently awarded the state's first Accelerated Translational Research Grant from the Cancer Institute NSW. The $4 million grant is part of the Accelerated Translational Research in Primary Liver Cancer program, and will bring together researchers, clinicians and experts across the state to improve liver cancer outcomes.

5B. Clinical II

Professor Patrick Schlegel

Professor and Head of Cellular Cancer Therapeutics, School of Medical Sciences / Medical Sciences Administration, Faculty of Medicine and Health, The University of Sydney; SCHN; Westmead Children's Hospital; CMRI

Professor Patrick Schlegel studied medicine at the Eberhard-Karls University of Tübingen then combined training as a clinician scientist with clinical duties at the University Children's Hospital Tübingen in the Department of Paediatric Haematology/Oncology and General Paediatrics. Professor Schlegel 's focus and major interests has since been in paediatric haematology, oncology, allogeneic stem cell transplantation, and immunotherapy. He held a consulting position in the Department of Paediatric Haematology/Oncology and Stem cell transplantation before being appointed by the University of Sydney in 2021 where he is currently Professor and Head of Cellular Cancer Therapeutics. His laboratories are based at the Children's Medical Research Institute and the Charles Perkins Centre, University of Sydney. His key focus in this role is to manage a clinical and translational CAR T cell program. Over the last few years Professor Schlegel has developed a novel Adapter CAR cell technology (AdCAR) that combines the flexibility of antibody-based anti-tumour therapy with the potency of CAR-mediated cancer treatment. The unique features of the AdCAR technology may overcome the major limitations of current CAR concepts. Research interests include innate immune-mediated anti-tumour response utilizing monoclonal antibodies and antibody constructs, T cell-mediated anti-tumour response via immune vaccine and bispecific T cell engagers and advanced CAR T cell technologies for cancer treatment and immunomodulation.

5B. Clinical II

Dr Inês Pires da Silva

Oncologist and Research Scientist at the Melanoma Institute Australia, Westmead & Blacktown Hospitals, and the University of Sydney

Inês Pires da Silva, MD PhD is a Medical Oncologist and Research Scientist at Melanoma Institute Australia, Westmead & Blacktown Hospitals, and The University of Sydney. Dr Pires da Silva received her MD degree at Universidade Nova de Lisboa (Portugal) in 2006 and her PhD in immune-oncology from New York University in 2016. Dr Pires da Silva completed a clinical fellowship at NYU (2014) in melanoma and completed specialist training in Medical Oncology at Instituto Português de Oncologia (Portugal) in 2016. Dr Pires da Silva has been working as a Medical Oncology and Postdoctoral research fellow at Melanoma Institute Australia and The University of Sydney since Sep/2016. Dr Pires da Silva is leading many translational research projects in the area of immunotherapy, including markers of response and mechanisms of resistance, that have been recognised by international organisations and/or published in high profile journals.

6. PLENARY: PATIENT EXPERIENCE & SOCIAL JUSTICE

Dr Ethan Basch

Richard M. Goldberg Distinguished Professor in Medical Oncology, Chief, Division of Oncology, Physician-in-Chief, NC Cancer Hospital; Professor, Health Policy and Management, UNC Gillings School of Global Public Health; Director, Cancer Outcomes Research Program, Lineberger Comprehensive Cancer Center; Co-leader, Cancer Prevention and Control Program, Lineberger, The University of North Carolina at Chapel Hill, USA

Dr Ethan Basch is Physician-in-Chief of the North Carolina Cancer Hospital and Chief of Oncology at the University of North Carolina, where he is the Richard M. Goldberg Distinguished Professor in Medical Oncology and Professor of Health Policy & Management. He has devoted his career to bringing the patient voice into cancer care delivery and drug development processes. His research group established that up to half of patients' symptomatic adverse events go undetected in clinical trials, and that patient-reported outcome questionnaires substantially improve detection. His team determined that integrating web-based patient-reported symptoms into oncology clinical practice improves clinical outcomes, including survival, and reduces health service utilization. His group created a system for the National Cancer Institute to collect patient-reported AEs during cancer trials called the 'PRO-CTCAE.' Dr Basch is involved in efforts to bring PROs into comparative effectiveness research, routine care, and quality improvement. He is a member of the Board of Directors of the American Society of Clinical Oncology (ASCO), an Associate Editor at JAMA, and a prior member of the Board of Scientific Advisors for the National Cancer Institute (NCI) and the Methodology Committee of the Patient-Centered Outcomes Research Institute (PCORI).

6. PLENARY: PATIENT EXPERIENCE & SOCIAL JUSTICE

Professor Fran Baum AO
Matthew Flinders Distinguished Professor; Director, Southgate Institute for Health, Society and Equity, Flinders Health and Medical Research Institute, College of Medicine and Public Health, Flinders University

Fran Baum is Matthew Flinders Distinguished Professor of Public Health and Foundation Director of the Southgate Institute for Health, Society and Equity at Flinders University, Adelaide, Australia. She received an Officer of the Order of Australia (AO) for her public health service. She is a Fellow of the Academy of the Social Sciences in Australia, the Australian Academy of Health and Medical Sciences and of the Australian Health Promotion Association. She is a past National President and Life Member of the Public Health Association of Australia. She Co-Chair of the Global Steering Council of the People's Health Movement – a global network of health activist (www. phmovement. org). She also served as a Commissioner on the World Health Organisation's Commission on the Social Determinants of Health from 2005-08. She holds grants from the National Health & Medical Research Council and the Australia Research Council which are considering health inequities and public policy, social determinants of health and health in all policies. Her book, The New Public Health (4th ed. published January 2016 Oxford University Press), is widely cited and used in many public health courses. Her latest book Governing for Health (Oxford University Press, New York, January, 2019) examines how a society can be best organised to promote health and equity.

(6) PANEL: SOCIAL JUSTICE IN CANCER CARE

Associate Professor Haryana Dhillon – *Panel Facilitator*
Co-leads the Survivorship Research Group and is a Director of the Centre for Medical Psychology and Evidence-based Decision-making, The University of Sydney

Associate Professor Haryana Dhillon (BSc MA PhD) is a Senior Research Fellow, who co-leads the Survivorship Research Group and is a Director of the Centre for Medical Psychology and Evidence-based Decision-making. She is passionate about rigor in research, collaboration, doing what she can to help humans make it to the 22nd century. Haryana's research is diverse but focused on helping people cope better and recover from the impact of cancer and its treatments.

Associate Professor Lisa Whop
National Centre for Epidemiology & Population Health, The Australian National University

Associate Professor Lisa Whop is a Goemulgal woman from the Wagadagam tribe of Mabuiag Island in the Torres Strait and was born and raised on the lands of the Bindal and Wulgurukaba peoples in Townsville North Queensland. She is Senior Fellow at the National Centre for Epidemiology and Population Health at The Australian National University. Associate Professor Whop has a Bachelor of Medical Science, Master of Applied Epidemiology and a Doctor of Philosophy (Epidemiology). She is Australia' s leading authority on cervical cancer control in Aboriginal and Torres Strait Islander women. Associate Professor Whop has extensive experience in Aboriginal and Torres Strait Islander health in research and health policy and has a background in skilfully translating research into policy and health practice. Although trained as an epidemiologist, Associate Professor Whop's program of work is focused on mixed methods implementation research. Associate Professor Whop is a chief investigator on several health-related grants and sits on high level policy committees. She is a recipient of a National Health and Medical Research Council Early Career Fellowship.

(6) PANEL: SOCIAL JUSTICE IN CANCER CARE

Professor Karen Canfell

Director, The Daffodil Centre; Professor & NHMRC Leadership Fellow, Faculty of Medicine and Health, The University of Sydney

Click here to read biography above

Professor Alex Broom

Professor, Sydney Centre for Healthy Societies, School of Social and Political Sciences, The University of Sydney

Alex Broom is Professor of Sociology and Director of the Sydney Centre for Healthy Societies, at the School of Social and Political Sciences, The University of Sydney. He is recognised as an international leader in sociology, with a specific interest in health and illness. His work takes a person-centred approach, qualitatively exploring the intersections of individual experience and social, political and economic context. His work uses highly innovative methodologies and theory to provide novel understandings of the social, cultural, political and economic underpinnings of the key health challenges, including cancer, palliative and end-of-life care. He is a global leader in empirically mapping and theorising patient, family and clinician perspectives of illness and care, offering a unique form of collaborative sociology that balances theory, empirical rigour and translatability. His overall aim is to draw on the lived experiences of all stakeholders in healthcare to improve experiences of illness and assist professionals in delivering better care. His recent books include: Dying (2015), Bodies and Suffering (2017,) and Survivorship (2021). In 2020 Alex established and directs the Sydney Centre for Healthy Societies - a research centre dedicated to harnessing social science and humanities expertise to understand and transform how health and social life intersect on our changing planet. Over the course of his career, he has been an investigator on over AU$18 million in competitive research grants, and has published over 250 publications including 14 books.

(6) PANEL: SOCIAL JUSTICE IN CANCER CARE

Professor Kelvin Kong

Otolaryngology, Head & Neck Surgeon (Ear Nose and Throat Surgeon); Honorary Professor: Macquarie University; Conjoint Associate Professor: University of NSW; Conjoint Associate Professor: University of Newcastle

Professor Kelvin Kong is an Aboriginal ENT surgeon who hails from the Worimi people of Port Stephens, north of Newcastle, NSW, Australia. He is now practising in Newcastle on Awabakal Country, specializing in Paediatric & Adult Otorhinolaryngology and Head & Neck Surgery. He is an active member of RACS and ASOHNS, having served on multiple advisory boards and committee's including the Indigenous Health and Fellowship Services Committee. He is currently serving as secretary of Australia and New Zealand Society Paediatric Otolaryngology (ANZSPO) and chair of Mina (Aboriginal and Torres Strait Islander Advisory Committee for RACS) and serves on Cancer Australia's Advisory board. Through his connections to the Hunter Medical Research Institute in Newcastle and the Centre of Research Excellence in Ear and Hearing Health of Aboriginal and Torres Strait Islander Children (Darwin), Kelvin conducts research into Aboriginal children's ear disease.

7. Consumer Focus

Ms Kathryn Leaney - *Plenary speaker, session co-chair and panel co-facilitator*
Member of the Executive Committee of Cancer Voices NSW and Manager of the Consumer Involvement in Research Program

Ms Leaney has been actively involved in cancer advocacy since 2013, following her own diagnosis of breast cancer. She wants to make sure that other people diagnosed with cancer do not have to go through the same experience she had. Ms Leaney appreciates the significant difference researchers make and the benefits that consumers bring to research teams for improved cancer outcomes of the future. She brings extensive experience as a member of Consumer Review Panels reviewing research grant applications on behalf of major funding organisations. She also has experience as a member of the Consumer Advisory Panel for the Translational Cancer Research Network (TCRN) based at the University of NSW. She helps researchers think about their work from the perspective of health care consumers, such as patients and their families.

Mr Murray McLachlan, *co-facilitator and session co-chair*
Deputy Chair, Cancer Voices NSW

Mr Murray McLachlan is a deputy chair of the executive committee of Cancer Voices NSW. Cancer Voices provides an independent voice for people affected by cancer in NSW, working to improve the cancer experience of the more than 50,000 people who will be diagnosed with cancer this year. He is also a board member of Health Consumers NSW which represents the interests of patients, carers and their families in NSW, a consumer representative in funding submissions for prostate cancer-related research, a consumer representative on the research committee of the Australian Prostate Cancer Research Centres, and on the Royal Australian and New Zealand College of Radiologists' Interventional Radiology Committee. Previously, he has also worked for the Cancer Council of NSW on the NSW Central Coast, focusing on policy and advocacy. His personal cancer experiences include the death of his long-term partner from pancreatic cancer in 2007, and successful surgical intervention for prostate cancer in 2009. Mr McLachlan's particular interest in Cancer Voices and Health Consumers NSW work builds on his professional life in the NSW public sector, influencing decision makers, policy development and implementation, and his involvement over many years with Sydney's LGBTIQ communities, including as president of Sydney Gay and Lesbian Mardi Gras and chair of Sydney Gay Community Publishing.

(7) PANEL: SUCCESSFUL CONSUMER-RESEARCHER COLLABORATION

Professor Lisa Horvath

Director of the Department of Medical Oncology, and Director of Research at the Chris O'Brien Lifehouse; Conjoint Chair of Medical Oncology (Genitourinary Cancers), Central Clinical School, The Universtiy of Sydney; Visiting Scientist, The Garvan Institute of Medical Research

Professor Lisa Horvath is the Director of Research at the Chris O'Brien Lifehouse. She is also the Professor of Medical Oncology (Genitourinary cancer) at the University of Sydney and Head of Advanced Prostate Cancer Research/Faculty member at the Garvan Institute for Medical Research. She is a clinician scientist, has an active clinical practice and is involved with a large number of clinical trials in prostate cancer in addition to phase I trial work. Having completed medical school at the University of Sydney and trained in medical oncology at Royal Prince Alfred Hospital, she subsequently worked at the Garvan Institute completing her PhD in translational research in 2004. She has published >120 original research papers in peer-reviewed journals in the last 20 years across the fields of cancer biology, biomarkers and clinical trials.

Mr Tony Maxwell

Westmead Prostate Cancer Support Group and Teleconference Support Group, consumer represetnative and advocate in multiple projects.

MrTony Maxwell (BSc, BA) is a consumer advocate for prostate cancer research. He is passionate about improving support services for the 25,000 men with advanced prostate cancer in Australia. He is also a consumer rep with many prostate cancer research projects and cancer research generally. Mr Maxwell is currently a member of the Westmead Prostate Cancer Support Group and Teleconference Support Group. He has been a councillor and Support & Advocacy Committee member for Prostate Cancer Foundation Australia (PCFA) and was awarded the Max Gardner Award for Distinguished Service by the PCFA in 2018. He sat on the Cancer Voices NSW Executive Committee from 2010 –2014 and is founding member and committee member of Advanced Prostate Cancer. He has been a consumer representative for multiple projects, review panels and awareness campaigns. He is
a father of 4 and a grandfather of 8 who has had a career in the paint industry and is also past president of ParrAssociateHills District Group and a Director of Australian Plants Society NSW.

(7) PANEL: SUCCESSFUL CONSUMER-RESEARCHER COLLABORATION

Associate Professor Lynnette Riley

Associate Professor, Sydney School of Education & Social Work, Program Director - Indigenous Studies & Aboriginal Education, FASS - Co-ordinator Indigenous Studies Major (ISM), The University of Sydney

Lynette Riley is a Wiradjuri & Gamilaroi woman from Dubbo and Moree; is an Associate Professor, in the Sydney School of Education & Social Work, The University of Sydney; and is Program Director for Indigenous Studies and Aboriginal Education. Associate Professor Riley trained as an infants/ primary teacher through Armidale CAE 1975-1977. She has been a classroom teacher in primary and high school; an Aboriginal Education consultant for schools; an Aboriginal Development Manager for VET; Manager of the Dubbo TAFE Campuses; State Manager for NSW DET, Aboriginal Education; and an academic at UNE and The University of Sydney. Her career focus has been on improving educational delivery for Aboriginal students and educating the wider public about Aboriginal people. Where possible, Associate Professor Riley incorporates her own cultural practices into her teachings.

Associate Professor Riley had her PhD conferred with ACU, in 2017, with her research on "Conditions of Academic Success for Aboriginal Students". Lynette seeks to create sustainable change for Aboriginal communities, through knowledge of cultural education and competence.

Associate Professor Riley currently sits on: Foundation for Breast Cancer Care, Member; NAIDOC Committee, Member; Aboriginal Languages Trust Board, NSW, Member; Aboriginal Affairs, OCHRE Research Governance Committee, Member; Yirigaa, Chair & Director.

Ms Karen Littlejohn

Executive Officer The Foundation for Breast Cancer Care

Following a successful career as a surgical nurse, Ms Littlejohn has dedicated much of her time in the pursuit of making a difference to the lives of others. She has done this through fundraising and marketing for a number of charities, including being a founding member of the Think Pink Ball held in Wagga Wagga, working closely with the Jane McGrath Foundation and the National Breast Cancer Foundation. Ms Littlejohn's most significant achievement was being instrumental in the placement of a McGrath Foundation nurse in Wagga Wagga. Country Hope, an organisation that cares for children with cancer and their families in the Riverina, has been another beneficiary of Karen's commitment. She has been involved with nursing care, mentoring, supporting and fundraising for the organisation over many years. She has worked on key projects with the Royal Australasian College of Surgeons, Provincial Surgeons Australia, Rural Craft Group and enters data for BreastSurgANZ Quality audit. Ms Littlejohn is a member of the Australian Institute of Company Directors, Fundraising Institute Women in Business, Wagga Business Chicks, and has a Masters in Business Administration.

(7) PANEL: SUCCESSFUL CONSUMER-RESEARCHER COLLABORATION

Ms Lillian Leigh

Non-Executive Director, and Membership & Advocacy Chair, Thoracic Oncology Group of Australasia

Following a lung cancer diagnosis in 2014, Sydney lawyer Ms Lillian Leigh shifted her focus to finding ways to improve outcomes of those affected by cancer. Lillian was appointed as an Advisory Council member of Cancer Australia in 2018, where she has also served on its Research and Data Advisory Group for three years. She is a non-executive director of the Thoracic Oncology Group of Australasia, an Executive Committee member of Cancer Voices NSW, a Patient Advisory Board member of Rare Cancers Australia, a Scientific Committee member of The ROS1ders (an international patient-driven organisation), and an appointed Mentor for the International Association for the Study of Lung Cancer's Supportive Training and Advocacy in Research and Science (STARS) Program.

Professor Nick Pavlakis

Professor of Medicine, University of Sydney; Board Chair, The Thoracic Oncology Group of Australasia (TOGA); Clinical Services Director, Genesis Care St Leonards, Frenchs Forest; Senior Staff Specialist, Department of Medical Oncology, Royal North Shore Hospital

Professor Nick Pavlakis is Senior Staff Specialist in the Department of Medical Oncology at Royal North Shore Hospital and conjoint Professor in the Faculty of Medicine University of Sydney. He is current Board Chair of the new Thoracic Oncology Group of Australasia (TOGA), member of the Upper GI Working Party of the Australasian Gastrointestinal Trials Group (AGITG) and is centre lead of the ENETS Centre of Excellence - RNSH NET service. He has extensive experience in clinical research leadership in national and international clinical trials in lung cancer, mesothelioma and GI cancers with several current and ongoing collaborative group trials in lung cancer, gastric cancer and NETs. As co-chair of the Bill Walsh Translational Research Laboratories he is involved in translational research in in lung cancer, pancreas and gastric cancers. Putting evidence into practice he has experience in systematic reviews and clinical practice guideline development.

8A. Drug development and new technologies

Dr Tristan Rawling

Discipline Leader of Chemistry and Senior Lecturer in the School of Mathematical and Physical Sciences at UTS

Dr Rawling completed a PhD in synthetic chemistry in 2009, followed by a Postdoctoral Research position at the University of Sydney working on drug discovery. In 2013 he returned to UTS after being awarded a Chancellors Postdoctoral Research Fellowship and in 2016 commenced his current academic position. His research combines chemical biology and medicinal chemistry approaches to drug design with a recent focus on development of novel anticancer agents that target cancer cell mitochondria. He has 48 papers and is an inventor on 4 patent applications, and has received research funding from the NHMRC and institution commercialisation grants.

8B. Supportive care and patient experience

Dr Jasmine Yee

Centre for Medical Psychology & Evidence-Based Decision-Making, Academic Fellow, Discipline of Exercise and Sport Sciences, The University of Sydney

Dr Yee is a postdoctoral research fellow at The University of Sydney. Her research focuses on supportive care for people with cancer, with a particular interest in the role of physical activity and exercise. She is also inaugural Terry Langbaum Survivorship Fellow of the Multinational Association of Supportive Care in Cancer (MASCC), leading international work to improve care and research for people living with advanced cancer.

8C. Cancer immunology

Dr Kavitha Gowrishankar
The University of Sydney, Westmead Institute for Medical Research

Dr Kavi Gowrishankar is a research fellow and emerging leader in the field of cell therapies. She is the lead basic scientist in the Micklethwaite laboratory, with over 20 years of technical expertise in cell and molecular biology. She has international work experience, having worked in renowned institutions in the US, India and Japan; However, describes herself as a Westmead product, having started her research career in Australia in WIMR, and after a couple of rewarding postdoc placements with the melanoma team, has now found her niche and passion in cell therapies. Kavi and Dr Micklethwaite have been developing several tools for universal applications of cell therapies. She has led the development of CAR T cells for multiple myeloma and is currently designing and developing various T cell receptors (native, transgenic and chimeric) for malignancy and infection, either as a direct lead or in a supervisory role or for collaborators. Designing novel receptors is becoming an addiction, she says. Her next goal is to extend cell therapies for solid tumours. She also delivers the immunotherapy lectures and workshops for the undergraduate cancer course (AMED) for USyd and is involved in curriculum development for SoMS.

9A. Precision medicine II

Dr Emily Colvin
Bill Walsh Translational Cancer Research Laboratory, Kolling Institute of Medical Research and The University of Sydney

Dr Colvin is an ovarian cancer researcher in the Bill Walsh Translational Cancer Research Laboratory at the Kolling Institute, University of Sydney. After completing her PhD in 2011 at the Garvan Institute in the area of biomarker discovery in pancreatic cancer, she moved to the Kolling Institute to focus on ovarian cancer research. She is currently the inaugural Proud Family Fellow and is a Director for the Australian Society for Medical Research. Her research aims to characterise the ovarian tumour microenvironment and its role in the initiation, growth and spread of ovarian cancer. She is currently working on understanding the role of non-coding RNA in ovarian cancer associated fibroblasts and how they are involved in ovarian cancer metastasis and immune evasion. She is also investigating novel therapies that alter the ovarian tumour microenvironment to see whether this is an effective way to treat ovarian cancer.

Professor Jean Yang
School of Mathematics and Statistics; Theme Leader for Integrative System and Modelling, Charles Perkins Centre, The University of Sydney

Professor Jean Yang a Professor of Statistics and Data Science at the University of Sydney and the Theme Leader of Integrative system and modelling at Charles Perkins Center. Her research stands at the interface between applied statistics and biology with focuses on the application of statistics to high dimensional problems in biomedical research. She was awarded the 2015 Moran Medal in statistics from the Australian Academy of Science in recognition of her work on developing methods for molecular data arising in cutting edge biomedical research. As a statistician who works in the bioinformatics area, she enjoys research in a collaborative environment, working closely with scientific investigators from diverse backgrounds.

9B. Psycho-Oncology

Professor Phyllis Butow AM
Psycho-Oncology Co-operative Research Group (PoCoG), School of Psychology, University of Sydney

Professor Phyllis Butow is an Emeritus Professor in the School of Psychology at the University of Sydney. She founded the Australian Psycho-Oncology Co-operative Research Group (PoCoG) and the Centre for Medical Psychology and Evidence-based Decision-making (CeMPED). Professor Butow has worked for over 30 years in health professional-patient communication and Psycho-Oncology. She has won many awards, including the International Psycho-Oncology Society Bernard Fox award for outstanding contribution to Psycho-Oncology research in 2009 and the Clinical Oncological Society of Australia Tom Reeve award for outstanding contribution to cancer care in 2011, was named NSW Cancer Researcher of the year in 2012 and received an Order of Australia (AM) in 2014. Professor Butow has conducted a large body of research on doctor-patient communication, patient involvement in cancer consultations and decision-making, patient and family support, management of fear of cancer recurrence, psychosocial issues in cancer genetics, and disparities in outcomes and needs of immigrants with cancer. Recently she has had a major interest in implementing evidence into practice, leading a program of work in implementing a clinical pathway for identifying and managing anxiety and depression in cancer patients (ADAPT).

Dr Rachel Campbell
Quality of Life Office, The University of Sydney

Dr Rachel Campbell is a Postdoctoral Research Associate at the Sydney Quality of Life Office, based at the University of Sydney. Her background is in health psychology research and her PhD focussed on examining psychological predictors of sleep disturbance and fatigue in individuals with a range of chronic health conditions. Her current research focusses on optimising the use of patient-reported outcome measures to assess and manage symptoms in oncology research and clinical practice, with the goal of improving people with cancers symptom burden and health-related quality of life.

9C. Medical radiation oncology

Professor Patrick Brennan
Professor of Diagnostic Imaging, The University of Sydney and CEO, DetectED-X

Professor Brennan's research explores novel technologies and techniques that enhance the detection of clinical indicators of disease, whilst minimising risk to the patient. He is recognised as a leader in clinical translation of medical imaging optimization and radiological perception. His research has been disseminated through 50 keynote/plenary talks across five continents and he has presented at the major international imaging meetings. He is the recipient of over 20 highly prestigious awards. He has published over 500 original papers in the highest ranked radiological journals along with the textbook Radiation Protection in Diagnostic X-ray Imaging (Jones and Bartlett Learning 2016). He has generated $34 million in funding from bodies such as the US National Institute of Health, European Union and a variety of Australian and New Zealand bodies. He has been the only recipient of two prestigious Honorary Fellowships from both Australia and Europe: the first ever Honorary Fellowship of the Australian Society of Medical Imaging and Radiation Therapy (2017); the third Lifetime Fellowship ever awarded by the Irish Institute of Radiography and Radiation Therapy. He has supervised over 50 higher degree students, and received multiple awards for supervision including the Vice-Chancellor's Award for Excellence. His work has been featured by most of the world's major news outlets including, ABC Radio, The Australian, The Sydney Morning Herald, London Telegraph, BBC Radio 4 and Irish Times. In 2018 he was awarded the Payne-Scott Professorial Distinction by the University of Sydney. He is Co-Founder and CEO of DetectED-X, a company aiming to improve cancer detection world-wide.

Professor Annette Haworth
Director of the Institute of Medical Physics, School of Physics, University of Sydney

Professor Haworth is the Director of the Institute of Medical Physics at the University of Sydney. Before taking up this appointment in 2016, Annette worked at the Peter MacCallum Cancer Centre as a clinical medical physicist and was involved in developing novel approaches for radiation therapy treatments for cancer patients. She now leads an international team of researchers involved in the application of quantitative imaging for radiation therapy applications.

Sydney Cancer Conference 2021

ABSTRACTS:

ORAL PRESENTATIONS

ABSTRACTS FOR ORAL PRESENTATIONS

Paper ID 15

Stability of multiparametric MR imaging biomarker-derived dose prescriptions for glioblastoma

Caterina Brighi[1]
David Waddington[1,2], Amy Walker[2,3,4,5], Lois Holloway[6,7,8,9], Eng-Siew Koh[2,3,4], Farhannah Aly[2,3,4] and Paul Keall[10]

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Background: Glioblastoma multiforme (GBM) is the most aggressive primary brain cancer carrying a poor prognosis, characterised by tumour recurrence only months after surgical resection and chemo-radiation using standardised target volume delineation for all patients. Personalised radiotherapy (RT) plans incorporating multiparametric MR (mpMRI) biomarkers may improve outcomes by identifying regions of infiltrating tumour (IT) *via* a tumour probability (TP) map. This would potentially allow selective RT dose escalation to biologically active tumour and healthy tissue sparing utilising a dose-painting (DP) approach.

Aim: This study evaluates the stability of mpMRI-based dose prescriptions based on DP with respect to the variations of the underlying imaging.

Methods: mpMRI data from a test-retest study was used to evaluate the stability of DP prescription maps for GBM in a MR-only treatment planning workflow. Publicly available data from The Cancer Imaging Archive of 11 newly diagnosed GBM patients acquired on two sessions prior to commencing adjuvant chemo-radiation was used. The voxel-wise TP of IT within the clinical target volume (CTV) margins was derived from image features with a logistic regression model, involving the linear combination of diffusion and perfusion MRI-derived parameters. A linear dose mapping function was applied to obtain a DP prescription map. The perfusion and diffusion MRI-derived parametric maps, TP and DP prescription maps were compared between the two MRI sessions and the intraclass correlation coefficient (ICC) within the CTV margins was calculated to quantify repeatability of the planning workflow.

Results and Conclusions: Median ICC values were 0.97, 0.69, 0.77, 0.75, 0.82, 0.92 and 0.96 for ADC, rBV, rBF, ADC-rBV TP, ADC-rBF TP, ADC-rBV DP and ADC-rBV DP maps, respectively. This study demonstrated that variations in mpMRI data in GBM patients do not affect the ability to generate consistent dose prescriptions when MRI-derived TP modelling is used in combination with dose-mapping techniques.

Paper ID 34

CBL0137 promotes CART-cell therapy against MLL-rearranged leukaemia

Mawar Karsa[1,2]
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Background: Despite remarkable improvements in the treatment of childhood B-cell precursor acute lymphoblastic leukaemia (BCP-ALL), prognosis remains dismal for infants with leukaemia harbouring a rearrangement of the Mixed Lineage Leukaemia (*MLL*/*KMT2A*) gene, with less than half of the patients surviving past 5 years. Chimeric Antigen Receptor (CAR)T-cell therapy that acts to program patient's T cells to destroy cancerous cells is now used to combat some types of CD19+ leukaemia and lymphoma. However, a significant proportion of BCP-ALL patients relapse after CART-cell therapy. Additionally, CD19 CART-cell therapy appears to be less effective against BCP-ALL with t(4;11) MLL rearrangements. Therefore, there is an urgent need to develop clinically relevant strategies to potentiate CD19 CART-cell therapy, particularly for MLL-rearranged BCP-ALL (MLL-ALL).

Aim: We previously showed that "chromatin damaging" therapy using small molecule inhibitor CBL0137 stimulates anti-tumour immune responses in solid cancer models. We therefore hypothesised that CBL0137 may promote CART-cell therapy by providing an immune environment that is more supportive for CART-cell functioning.

Methods: Human T cells were retrovirally transduced with the 3rd generation of CARs providing CD28- and OX40-co-stimulation. Patient-derived xenograft (PDX) model of infant MLL-ALL was used to examine anti-tumour activity of CD19 CART-cell therapy in mice primed with CBL0137. High-through flow cytometry was used for the simultaneous measurement of CART-cell markers and cytotoxicity against leukaemia.

Results and Conclusions: Using a PDX model of infant MLL-ALL, we have shown that CBL0137 given 1 day prior to CART-cell infusion, delayed leukaemia growth and promoted CART-cell expansion and effector function. An inverse correlation between %CD19+ leukaemia cells and %CD3+ T cells in the blood of mice primed with CBL0137 and treated with CART-cells was observed. Priming with CBL0137 induced a pro-immunogenic environment through upregulation of interferon signalling. The "chromatin damaging" agent CBL0137 could represent a novel therapeutic option to potentiate CART-cell therapy for MLL-ALL.

Paper ID 36

Canteen Connect: The evaluation of an online health community for AYAs impacted by cancer

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Background: Adolescent and young adult (AYAs) impacted by their own or a familiar cancer diagnosis cancer have a higher incidence of distress than their peers and high levels of unmet needs, contributing to their distress. AYAs impacted by cancer require information and peer support throughout the cancer journey to ameliorate feelings of isolation. Online Health Communities (OHC) provide social networks, support and health-related content to people united by a shared health experience. Canteen Connect, an OHC was developed for young people impacted by cancer, providing access to peer support groups, online counselling sessions, and psycho-educational resources.

Aims: To assess the acceptability and effectiveness of Canteen Connect, an online health community for young people impacted by their own or familial cancer.

Methods: Using the Implementation Outcomes Framework, a cross-sectional quantitative questionnaire assessed the acceptability, appropriateness and effectiveness of Canteen Connect. Participants were 120 current AYA (12-25 years) users of Canteen Connect (mean age=19.3 years).

Results: Participants found Canteen Connect acceptable, with high agreement that it was helpful (76%), interesting (76%) and easy to use (71%). Canteen Connect was appropriate and useful for connecting with young people like themselves (74%); chatting with a counsellor (84%); and finding information about their cancer experience (62%). Three-quarters of participants felt they received emotional support from other young people in the Canteen Connect community. For participants who had experienced issues with sadness, worry, or anxiety in the past month due to their cancer experience, two-thirds reported a positive impact on their feelings after using Canteen Connect (73%, 66%, and 65%, respectively).

Conclusion: An innovative new OHC, Canteen Connect fills an important service provision gap for young people impacted by cancer, with initial promising psychological outcomes. Participant feedback will inform ongoing development of Canteen Connect and long-term psychosocial impacts are currently being measured.

Paper ID 38

Patient-derived xenograft (PDX) mouse models to test novel cell therapies for leukemia

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Background: Adoptive cell therapy using T lymphocytes genetically modified with tumor-targeting chimeric antigen receptors (CAR) is a potent and potentially curative treatment for leukemia and lymphomas.

Aims: Patient-derived xenograft (PDX) models are used to screen different T-cell therapy treatments in specific preclinical settings, study potential improvements to cell therapies (ex vivo expansion, genome editing, safety switches), examine the heterogeneity in patient responses, determine mechanisms of resistance, and test combination therapies.

Methods and Results: By testing CD19-specific CARs (CAR19T) engineered by Dr. Micklethwaite's team from WIMR using PDX mouse models of B-cell precursor acute lymphoblastic leukemia (BCP-ALL), we showed that sustained activity of CAR T-cells depends on CAR structure. Using 4-1BB instead of CD28 co-stimulation resulted in greater potency and persistence of CAR19T cells and provided protection against leukemia re-challenge even at diminishing doses. Our PDX models showed that relapse with CD19 antigen loss can occur despite initial tumor clearance. $CD19^-$ variants have been identified in all PDXs before CAR T-cell treatment, and outgrowth of $CD19^-$ variants was observed in mice treated with CAR19T cells. CAR T-cell persistence in mice infused with high doses of effector cells correlated with increased proportions of $CD19^-$ relapses. Our data suggest that CD19 isoforms lacking the sequences needed for CD19 cell surface expression (critical for targeting by CAR19T cells) in leukemia blasts naturally exist in BCP-ALL pediatric patients before treatment and are selected under CAR19T cell pressure. In addition to $CD19^-$ relapses, a proportion of mice relapsed with $CD19^+$ disease that correlated with the lack of CAR T-cell persistence. Transcriptome profiling of individual PDXs has identified patient-specific biomarkers associated with long-term persistence of CAR T-cells.

Conclusions: Preclinical testing of novel immunotherapies in PDX models provides valuable insights into mechanisms of CAR T-cell persistence and $CD19^{+/-}$ relapses that will improve CAR design for better patient outcomes.

Paper ID 39

Improving physical activity levels among childhood cancer survivors: A digital educational program

Lauren Ha[1,2]
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Background: Many childhood cancer survivors achieve insufficient physical activity (PA) levels. Perceptions of PA and fitness levels may have a strong influence on engagement in health behaviours. Understanding objective PA levels may assist in the development of interventions.

Aim: This study explores survivors' perceptions of their PA and fitness levels, and their objective PA levels using accelerometry. We then tested the feasibility of a digital educational intervention, 'iBounce'.

Methods: We recruited 116 survivors aged 8-18 years. We assessed their perceived PA and fitness levels using questionnaires and compared their perceptions with the PA guidelines (≥420 min/week moderate-vigorous PA [MVPA]) and 6-minute walk test (6MWT) percentiles, respectively. A sub-group of survivors (n=38) wore an accelerometer (GeneActiv) for seven consecutive days. We developed 'iBounce', a 12-week digital PA intervention consisting of an online program and wearable activity trackers, currently being piloted in survivors aged 8-13 years.

Results: One-third of survivors incorrectly perceived their PA levels as appropriate (84% underestimated, while 16% overestimated the appropriateness of their PA levels). Survivors achieved mean 244.3±168.1 min/week MVPA and achieved mean 1.3±1.7 days of at least 60min MVPA per week. Survivors were most active during school hours (9am-3pm) compared to before and after school. Survivors were sedentary for a mean of 5±2 hrs/day, excluding sleep time (range=2-9hrs). To date, 30 survivors have opted into the iBounce pilot (46.7% female, mean age: 10.2 years). Eleven survivors have completed the program, with the remaining survivors' mid-way through the program (n=8 dropouts). iBounce participants appear to have improved 6MWT distance post-intervention ($p<0.001$).

Conclusions: Childhood cancer survivors may have inaccurate perceptions regarding the appropriateness of their PA and fitness levels. Survivors are most active during school hours, suggesting potential intervention opportunities before/after school to further increase their PA levels. iBounce appears to be feasible and may be a promising program to improve PA in survivors to ultimately improve their fitness and reduce their risk of cardiometabolic complications.

Paper ID 45

Targeting NDRG1 to inhibit bi-directional oncogenic cross-talk between pancreatic cancer and stroma

Bekesho Geleta[1]
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Background & Aims: Pancreatic cancer (PaCa) is characterized by a dense stroma surrounding the tumor cells composed of mainly pancreatic stellate cells (PSC), which are activated by Sonic hedgehog (SHH) produced by PaCa cells. In turn, activated PSCs release cytokines and growth factors such as hepatocyte growth factor (HGF), insulin-like growth factor (IGF-1) and interleukin 6 (IL-6) that stimulate proliferation and metastatic ability of PaCa cells. N-myc downstream regulated gene 1 (NDRG1) is a metastasis suppressor and potent inhibitor of numerous oncogenic signaling pathways in PaCa cells. We hypothesized that targeting NDRG1 using the novel clinically-trialed anti-cancer agent, di (2-pyridyl) ketone 4-cyclohexyl-4-methyl-3-thiosemicarbazone (DpC), may interrupt the oncogenic cross-talk between PSCs and PaCa cells.

Methods: We examined the effects of NDRG1 and DpC on: ***(i)*** HGF and IGF-1 receptor activation and down-stream signaling in PaCa cells; ***(ii)*** PaCa mediated production of SHH; ***(iii)*** Activation of PSCs and their ability to produce HGF, IGF-1 and IL-6. To assess the tumor-stromal interaction, we used PSC and AsPC-1 conditioned media, 3D co-culture spheroids and an orthotopic *in vivo* model that incorporates both PaCa cells and PSC cells.

Results: We demonstrate that DpC potently inhibits activation of HGF and IGF-1 pathways in PaCa cells, with this effect being dependent on NDRG1. DpC also inhibited SHH signaling and PSC activation, leading to reduced production of HGF, IGF and IL-6 by these stromal cells. *In vivo*, DpC markedly reduced PaCa tumour growth and metastasis, being more effective than gemcitabine.

Conclusion: Targeting NDRG1 with DpC can interrupt the bi-directional cross-talk between PaCa and PSCs, breaking the oncogenic cycle that promotes desmoplasia. This presents a unique and innovative opportunity to overcome the desmoplasia of PaCa and constitutes a novel approach to overcoming PaCa progression and metastasis.

Paper ID 54

Investigating Novel Treatments to Improve Radiation Response in Diffuse Intrinsic Pontine Glioma

Faiqa Mudassar[1]
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[8] Blacktown Hematology and Cancer Centre, Blacktown Hospital

Background: Diffuse intrinsic pontine glioma (DIPG) is an incurable pediatric brain tumor with a median survival of 12 months. Current management is limited to radiotherapy; however, the tumor recurs secondary to radioresistance. Tumor hypoxia appears to be one of the major contributors to radioresistance of DIPG, as oxygenation is critical to successful radiotherapy treatment. Therefore, strategies to alleviate hypoxia could enhance the effectiveness of radiotherapy and result in improved survival outcomes of patients with DIPG. Recent approaches to target tumor hypoxia are predicated on inhibiting mitochondrial respiration of the tumors to decrease oxygen consumption rate (OCR) and increase oxygenation.

Aims: Here, we aimed to identify a safe but potent mitochondrial inhibitor that could decrease OCR and hypoxia, and improve the radiosensitivity of DIPG.

Methods: A subset of anti-parasitic drugs (atovaquone, ivermectin, quinacrine, mefloquine and proguanil) which are known mitochondrial inhibitors were studied against a panel of patient-derived DIPG cell lines. We assessed their antiproliferative effects, OCR inhibition and radiosensitising efficacy using cell proliferation, extracellular flux and colony formation assays.

Results and conclusions: Among the five tested drug candidates, atovaquone was found to be the most potent OCR inhibitor with minimal antiproliferative effects on DIPG cultures. It also decreased hypoxia in 3-dimensional DIPG neurospheres, reduced the expression of hypoxia-inducible factor-1a and improved the radiosensitivity of neurospheres of DIPG. Its anti-mitochondrial role was further confirmed by inhibition of various mitochondrial parameters and increase in reactive oxygen species. Overall, these results provide promising *in vitro* evidence of atovaquone as a hypoxia modifier and radiosensitiser in DIPG and pave a way for rapid translation to *in vivo* studies.

Paper ID 66

Health literacy and cancer care coordination among patients with head and neck cancer

Rebecca Venchiarutti[1,2]
Jonathan R Clark[1,2,3], Carsten E Palme[1,2,3] and Jane M Young[2]
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Background: Poor health literacy (HL) has been associated with worse access to health care services, higher morbidity and mortality, and lower satisfaction with care. To our knowledge, the association between HL and coordination of cancer care has not been examined in patients with head and neck cancer (HNC).

Aim: To explore the correlations between domains of patient-reported HL and experiences of cancer care coordination.

Methods: Patients who underwent treatment for HNC at one of four sites in NSW were invited to participate. Patients completed two questionnaires: 1) the Health Literacy Questionnaire® (HLQ®), a 44-item validated tool assessing HL across nine domains, and six months post-treatment, 2) the Cancer Care Coordination Questionnaire for Patients (CCCQ-P), a validated tool measuring care coordination across two domains (navigation and communication). A total score is also obtained by summing scores from the two domains. Non-parametric correlations between the CCCQ-P domains and total scores with HLQ® domains were assessed using Spearman's rank-order correlation coefficient. Linear regression was used to examine associations between patient and clinical factors with care coordination scores.

Results: From October 2018-March 2020, 97 of 131 invited patients completed the HLQ®, 79 of whom completed the CCCQ-P (65% male; mean age 64 years). All of the nine HLQ® domains were significantly positively associated with the total CCCQ-P score, and eight of the nine HLQ® domains were significantly positively associated with both the navigation and communication domains of the CCCQ-P. Almost half of patients surveyed (38/79; 48%) reported a problem meeting the financial costs of cancer. Univariable linear regression analysis found no patient or clinical factors that were associated with care coordination scores.

Conclusion: Our findings demonstrate HNC patients with higher HL report better coordination of cancer care. Health policy should focus on promoting a navigable cancer care environment for persons with low HL.

Paper ID 71

Targeting chromatin potently inhibits leukaemia progression in MLL-rearranged leukaemia models

Lin Xiao[1,2]
Mawar Karsa[1,2], Emma Ronca[1], Angelika Bongers[1], Weiman Gao[1,2], Angelika Kosciolek[1], Ali El-Ayoubi[1], Murray Norris[3], Michelle Haber[3] and Klaartje Somers[1,2]
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[3] Children's Cancer Institute

Background: Infant acute lymphoblastic leukaemia (ALL) is highly aggressive with five-year survival rates below 50%. Approximately 70% of infant ALLs harbour rearrangements of the mixed-lineage leukemia (*MLL* or *KMT2A*) gene which drive rapid disease progression through genetic and epigenetic dysregulation. Recently studies have suggested that epigenetic aberrations in *MLL*-rearranged (*MLLr*-) ALL represent attractive targets for developing effective and safe therapies.

Aim: To develop a translatable combination strategy using two chromatin-targeting drugs, CBL0137, a nongenotoxic agent currently in clinical trials for haematological malignancies, and panobinostat, an FDA-approved pan-histone deacetylation inhibitor, in *MLLr*-ALL animal models.

Methods and Results: Treatment of multiple *MLLr* leukaemia cell lines with CBL0137 and panobinostat combination synergistically reduced colony formation by 80% and significantly induced apoptosis at as early as 24 hours. Notably, the combination significantly inhibited regulators associated with chromatin functions including genes regulating histone assembly and cell cycle. Immunocompetent transgenic *MLL*-AF9 mice resembling a highly aggressive clinical *MLLr*-ALL subtype were treated with 60 mg/kg of CBL0137 (p.o., twice/week) and 7.5 mg/kg of panobinostat (i.p., 5 days/week) either as a single agent or in combination (n=6/group). The treatment was well tolerated with minimal toxicity. While both single agents demonstrated significant efficacy, the combination reduced leukaemia burden by more than 10-fold and extended survival more effectively than either drug alone. Promisingly, in a patient-derived xenograft *MLLr*-ALL (MLL6) model (n=8/group), the therapeutic enhancement of the CBL0137 and panobinostat combination was even more pronounced. The median event-free survival rate was markedly prolonged in the combination group by 40% and 78% compared to that in CBL0137 or panobinostat single-agent treatment groups, respectively.

Conclusion: The CBL0137 and panobinostat combination is highly effective in inhibiting disease progression in aggressive *MLLr*-ALL models. Given both agents currently being tested in clinical trials, this combination represents a promising translatable strategy for childhood *MLLr*-ALL.

Paper ID 78

Aggressive breast cancer subtype eats tryptophan!

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Background: Immunotherapy has been proposed as a treatment to stop breast cancer (BrCa) progression. However, there has been limited success in this treatment. This implies that BrCa tumors have another immune evasion mechanism(s). While the kynurenine pathway (KP) is known to be a key player mediating tumor immune evasion and shown to have a potential role in cancer, little is known about KP involvement in BrCa.

Aims: This study aims to fully characterize the activity of the KP in each BrCa subtype and to investigate whether variations in serum KP parameters are associated with particular BrCa clinical subtype.

Methods: To understand how KP is regulated in BrCa, we examined the KP profile in BrCa cell lines (n=7) and clinical samples (n = 1,997) that represent major subtypes of BrCa (luminal, HER2-enriched, and triple-negative (TN)). We carried out qPCR, western blot/immunohistochemistry and ultra-high pressure liquid chromatography to quantify KP enzyme gene, protein and activity respectively.

Results: We revealed that the KP is highly dysregulated in the HER2-enriched and TN BrCa subtype. Our multi-omics approach has shown that the KP enzymes KMO and KYNU are highly upregulated in the HER2-enriched and TN BrCa subtype, leading to increased production of the potent immunosuppressive metabolite, 3-hydroxylanthranilic acid.

Discussion: Our data indicate that KP is dysregulated in all BrCa and may be the major facilitator in the evasion of immune surveillance in TN BrCa. Significantly, our study shows that serum KP profiles can successfully discriminate TN BrCa patients from other BrCa patients.

Translational significance: Our work will highlight the role of KP in BrCa, and potentially identify a new blood-based biomarker to identify triple-negative BrCa patients.

Paper ID 81

Knowledge and screening practices of cervical cancer among migrant women living in Sydney, Australia

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Background: In Australia, cervical screening participation rates remain low amongst migrant women. There is limited research on the barriers and facilitators that influence migrant women and their cervical screening behaviours in Sydney, Australia. Moreover, this is the first study that explores the factors that play a role amongst migrant women from Middle Eastern, South East Asian and African backgrounds living in Sydney, Australia.

Aims: The aim of this study is to describe the attitudes, beliefs, knowledge and awareness of cervical cancer screening and screening practices amongst migrant women living in Sydney, Australia.

Methods: Fifty-two women (30 South-East Asian, 12 Middle Eastern & 10 African) were recruited using two non-probabilistic sampling methods, convenience and snowball sampling. Participants were recruited through migrant community centres and organisations. Data was collected through Focus Group Discussions (FGDs). The FGDs were audio-recorded and verbatim transcribed. The data were analysed using thematic analysis.

Results: This study found that migrant women living in Sydney displayed a lack of awareness and knowledge about cervical cancer and screening practices. Individual and system-level barriers and facilitators that influenced screening attendance were identified. The results revealed that African migrants were less likely to be aware of cervical cancer and screening compared to South-East Asian and Middle Eastern women. Our findings also revealed that long-term migrants were more aware of the available health services. It was also established that effective communication between migrant women and health providers is lacking. Cultural barriers play a major role in cervical screening participation due to the stigma associated with cervical screening within all cultures.

Conclusions: To increase cervical cancer screening uptake of migrant women living in Sydney, culturally appropriate education programs and health promotion strategies targeted towards different ethnic groups need to be administered.

Paper ID 90

Overcoming the chemoresistance mechanisms in pancreatic cancer via targeting the AMPK energy pathway

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Background: Patients with pancreatic ductal adenocarcinoma (PDAC) are often diagnosed in late stages, featuring advanced tumours that are highly resistant to current chemotherapeutic options. The identification of pathways associated with chemo-resistance could be vital in the search for better treatment options against PDAC.

Aims: To understand the mechanisms involved in the development of chemo-resistance in PDAC and to develop a novel therapy to overcome chemo-resistance.

Methods: Wild-type (WT) PDAC cell lines were sequentially incubated with increasing concentrations of standard PDAC chemotherapeutic gemcitabine to select a chemo-resistant (GR) phenotype. Chemo-resistance was confirmed by cell viability assays (MTT and CFA). Untargeted mass spectrometry-based proteomic analysis was performed on WT and GR cell lysates and was bioinformatically analysed to identify key upstream targets involved in mediating chemo-resistance. ^{1}H-NMR analysis was performed on the medium collected from cultured WT and GR cells. Further studies targeting the identified key upstream pathway, involving AMPK, were performed to determine its ability to overcome chemo-resistance.

Results: There was a significantly higher IC50 for gemcitabine in GR compared to WT cells in both cellular proliferation (4,500-fold) and colony formation (2333-fold) assays. Proteomic analysis identified and quantified 6139 proteins. There were 1615 significantly ($p < 0.05$) upregulated (865 proteins) or downregulated (750 proteins) proteins in GR compared to WT cells. AMPK was shown to be a key upstream regulator which was significantly activated in GR cells. Metabolomics data demonstrated an energy deprived phenotype in GR cells, emphasizing the role of AMPK as a critical energy homeostasis pathway. Inhibitor compounds targeting the AMPK pathway (i.e., SBI-0206965) demonstrated synergistic activity with gemcitabine in GR cells, indicating a re-sensitization to chemotherapy.

Conclusions: AMPK could be a major regulator of chemoresistance in PDAC. The synergy and anti-tumour activity of novel AMPK inhibitors in chemo-resistant PDAC cells indicate a potential chemotherapeutic strategy against seemingly untreatable advanced PDAC tumours.

Paper ID 96

Identifying and targeting novel immunosuppressive driver mechanisms in young melanoma patients

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Background: There is a current lack of effective treatment for advanced stage adolescents and young adults (AYA) melanoma patients aged 15 to 30 years. Cancer therapies that target cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) or programmed cell death protein 1 (PD-1) pathways has improved the 5-year overall survival from less than 5% to 50%. However, AYA patients are less responsive to immunotherapy due to their unique genomic biology and clinicopathological differences when compared to those of older patients. Identifying immunosuppressive driver genes and novel drug targets may improve treatment strategies for these patients.

Aim: The primary aim of this study was to determine the distinct immunogenic patterns of treatment response and immunosuppressive microenvironment present in the melanoma biopsies of AYA patients.

Methods: Whole transcriptome sequencing, advanced bioinformatics and multiplex immunofluorescence were performed on formalin-fixed paraffin-embedded melanoma tumour tissue samples (n=75) taken at baseline from AYA patients treated with anti-PD-1 and/or anti-CTLA-4 immunotherapy.

Results: The AYA tumours demonstrated high infiltration of regulatory T cells when compared to the adult melanomas (median = 13.1 versus 0.815 cells/mm2, 95% confidence interval (CI): 7.86–28.7 versus 0.468–1.447; P-value < 0.0001). Immune deconvolution demonstrated infiltration of tumour-associated macrophages (median = 9.57%, 95% CI: 5.78–12.3%; P-value < 0.05), and lower proportion of cytotoxic CD8 T cells in AYA tumours compared to adult tumours (median = 0.031% versus 3.36%, 95% CI: 0–1.48% versus 2.32–5.80%; P-value = 0.0036). Down-regulated genes (CD3D/E/G, CD8A, CXCL9 and TIGIT; adjusted P-value < 0.05) were implicated in antigen processing and presentation signalling and chemokine pathways, suggesting AYA tumours can camouflage and hide from immunotherapy treatment by altering the tumour microenvironment or secreting immune suppressive cytokines.

Conclusions: Novel treatment strategies focused on targeting the microenvironment may improve the effectiveness of cancer immunotherapies in advanced stage AYA melanoma patients.

Paper ID 99

A Three-Dimensional Computational Model of Prostate Cancer Biology

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Background: Incorporating biological information in planning and delivering treatment may improve outcomes for prostate cancer patients. This is feasible with multiparametric MRI (mpMRI), from which machine learning models can predict the location of tumour lesions. Previous studies have shown that population-based models can improve predictive accuracy. We extend this idea by incorporating additional biological characteristics such as tumour grade and tumour cell density.

Aim: Our aim is to generate a probabilistic atlas: a population-based model of tumour location and biological characteristics, to be used with mpMRI to aid biologically-optimised RT planning.

Methods: This study recruited 70 men scheduled for radical prostatectomy. After surgery, each prostate specimen was set in a custom sectioning box prior to *ex vivo* MRI acquisition. Histology slides were taken at locations corresponding to MRI slices. A pathologist annotated and graded tumour lesions, and pixel-level cell density was calculated. Landmark-based registration mapped these data to the MRI.

Our atlas model requires co-registered patient data. A reference was constructed using average prostate, peripheral zone, and urethra volumes, to which patient data were registered with a novel anatomy-guided DIR process. In this reference space, the tumour location and grade data, and cell density maps were aggregated.

Results: Cell density was highest in the lateral posterior prostate region, reaching 35000 cells/mm^3. Tumour probability was also highest in these regions, approaching 40%. The biological atlas can be stratified by tumour grade and patient-specific measurements such as PSA serum level.

Conclusions: The probabilistic biological atlas provides a quantitative 3D model of the location and characteristics of prostate cancer in the study cohort. A registration framework has been designed to map the atlas to patient MRI.

Translational significance: Results of this study will be used to investigate personalised, biologically-optimised RT, including the potential benefit of emerging treatment modalities such as proton therapy.

Paper ID 100

Integrated Molecular Analysis of Polyps (IMAP) study to understand how bowel polyps develop

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Background: Bowel polyps are pre-cancerous cell clusters in the colorectum that carry genetic lesions, giving potential to develop into bowel cancers. In contrast to colorectal tumours, less is known at a molecular level about these premalignant lesions. Molecular information may be useful to develop more effective prevention strategies and as biomarkers to optimise clinical practices.

Aim: This study aims to carry out molecular landmarking of bowel adenomas, integrating clinical, genetic, proteomic, immune and microbiome data from patients undergoing colonoscopy.

Methods: 170 colonoscopy participants have been enrolled in the IMAP study (50 polyp patients, 120 non-polyp patients). Biopsies paired with matched germline DNA underwent whole exome sequencing (WES) on NextSeq via SureSelect Human All Exon V7 capture kit. Mucosal biopsies adjacent to polyps were used for 16S microbiome sequencing. Multiplexed immunohistochemistry was used to phenotype immune cells in polyps and adjacent mucosa.

Results: WES of 36 adenomas identified canonical cancer driver genes with high prevalence including APC (50%), MUC16 (22%), SYNE1 (19%), CTNNB1 (19%), and BRAF (19%). Median somatic mutation burden in large tubular adenomas (>= 10mm) was 4.62/Mb, which was higher than the median burden of 3.52/Mb in small tubular adenomas. Interestingly, some small adenomas had high mutational burdens compromising the function of tumour suppressors and could be considered at high-risk for malignant transformation. We observed enrichment of certain bacteria *Megamonas, Fusobacterium varium, Tissierellales* and *Megasphaera* in cases with polyps compared to polyp-free patients. Bacteria associated with *Lachnospira, Coprococcus comes, Christensenellaceae* and *Eubacterium* were typically depleted in cases with polyps compared to controls. Immunophenotyping revealed a reduction in macrophage and dendritic cell density in polyp tissues compared to adjacent mucosa. No significant changes were observed with lymphocytes.

Conclusions: Preliminary findings highlight the clinical potential of detailed molecular characterisation of bowel polyps. Mutational burden, microbiome and immune features may be exploited as diagnostic and prognostic biomarkers for patient management.

Paper ID 107

Female hormonal factors and lung cancer death in never-smokers: results from China Kadoorie Biobank

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Background: There is growing, but inconsistent, evidence suggesting endogenous/exogenous oestrogens may play a key role in lung cancer (LC) development, especially among never-smoking women for whom LC risk factors remain largely elusive.

Aim: To assess the association between several female reproductive and hormonal factors and LC mortality among never-smokers.

Methods: The China Kadoorie Biobank is a large-scale prospective cohort, with 302,510 women aged 30–79 years recruited from ten regions in China during 2004-2008. We assessed the risk of LC death among self-reported never-smoking cancer-free women at recruitment, in relation to age at menarche, age at menopause, time since menopause, prior use of oral contraceptives (OCP), number of livebirths, breastfeeding and age at first livebirth. Women were followed up to 31/12/2016 with linkage to mortality data. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox regression with adjustment for key confounders including known LC risk factors such as household air pollution and second-hand smoke.

Results: There were 814 LC deaths among 287,408 never-smoking women with a median follow-up of 10.3 years and median age of 50.5 years at recruitment. Compared with never-users of OCP, women who had used OCP within 15 years prior to baseline had a significantly higher hazard of LC death (HR=1.85; 95% CI 1.14-3.00); in contrast, the difference was not significant for those who used OCP 15+ years before baseline (HR=1.13; 95% CI 0.88-1.44). Among OCP ex-users, the hazard increased by 6% with each additional year of use (HR=1.06; 95% CI: 1.01-1.10). Among parous women, each single livebirth was associated with a 12% increased hazard of LC death (HR=1.12; 95% CI: 1.03-1.21) and among post-menopausal women, each year since menopause was associated with 2% increased hazard of LC death (HR=1.02; 95% CI: 1.01-1.04).

Conclusions: These results suggest that factors that affect oestrogen levels, e.g. recent or longer duration of OCP use, could play a role in lung carcinogenesis. Further work is required to establish clinical significance.

Paper ID 112

Australian multiple myeloma incidence and mortality trends from 1982-2016 and projections to 2040

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Background: Improved diagnostics and new treatments for multiple myeloma (MM) have prolonged survival, but MM remains largely incurable. The management of MM is expensive and expected to increase. To date there have been limited studies on MM past trends and no long-term projections in Australia.

Aim: To analyse past trends in MM incidence and mortality and project the future disease burden in Australia to 2040.

Methods: We examined the past trends in MM incidence and mortality rates, using national incidence and mortality data for 1982 to 2016. The rates are projected to 2040 using age-period-cohort models and were standardised to the 2001 Australian population. We estimated the future numbers of cases and deaths by applying the rates to the Australian Population Projections.

Results: Projections based on the increase in age-standardised incidence rates observed for MM (4.7/100,000 in 1982 to 6.9/100,000 in 2016) indicate rates of 7.6/100,000 by 2040, with similar pattern across all age groups. The number of new MM cases are expected to increase by 81% from 1,993 in 2017 to 3,601 in 2040. The age-standardised mortality rates were relatively stable over the period 1982-2016 (3.0/100,000 in 1982 and 3.2/100,000 in 2016) and are projected to decline from 3.1/100,000 in 2017 to 2.4/100,000 in 2040. The rate decrease is expected to be most pronounced for older age groups 70+ years (24.8/100,000 in 2017 to 18.5/100,000 in 2040). However, the total number of MM deaths is expected to increase by 36% from 921 deaths in 2017 to 1,252 deaths in 2040.

Conclusion: MM incidence rates are projected to increase with the percentage increase in future cases substantial, while mortality rates are projected to decrease. Recent developments have transformed MM into a chronic cancer with survivorship considerations. Planning for prolonged, expensive, complex treatment and care will be key. Research on preventive strategies should also be prioritised.

Paper ID 118

High-dimensional and spatial analysis reveals immune landscape dependent progression in carcinoma

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Background: Head and Neck Cutaneous Squamous Cell Carcinoma (HNcSCC), or 'non-melanoma skin cancer', has a mortality rate that is 8th among all cancers. Risk-factors for cSCC include UV exposure, immune suppression, smoking and Human Papilloma virus (HPV) status.

Aim: To understand the role of tumour immune microenvironment at different stages of cSCC .

Methods: High-dimensional Imaging mass cytometry (IMC) was utilised to examine more than 38 different parameters in the Tumour microenvironment (TME) of primary and metastatic tumours. Tumour biopsy specimens taken from 32 HNcSCC patients were separated into primary tumours that never progressed (NP, n=9), Primary tumours that progressed (P, primary, n=8) and metastatic tumours of patients who progressed (P, Met, n= 20).

Results: We found significant differences in the immune composition of primary tumours that never progressed compared to primary tumours that progressed. Tumours with favourable outcomes were generally characterised by active T cell responses. We also found differences in the immune landscape as tumours progressed from primary to metastasis, with increased expression of many checkpoint receptors. Mapping of cellular interactions revealed a complex picture, with many immune cell interactions that were associated with clinical outcomes.

Conclusions: Mapping the immune landscape of human tumours could provide insight into the role of immune cells in disease progression. Our data suggests that the immune composition of primary tumours can predict clinical outcomes. In depth investigation into the immune environment of primary HNcSCCs has demonstrated that there are significant differences in the primary tumours of HNcSCC patients that progress and those that do not. The findings of this research offers a clear pathway to determine clinical outcomes based on a patients TME signature. This could also be extended to predicting who should be on immunotherapy and the chances of success of these therapies. Importantly, if progression to poor outcomes can be predicted, this could lead to a more tailored approach, with improved clinical outcomes and lower health burden.

Paper ID 120

Systemic myeloid cells and local T cells propel immunotherapy-induced colitis

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Backgrounds: While immunotherapy has revolutionised cancer care, it also often leads to immune activation in normal host tissue, resulting in immune-related adverse events (irAEs). Such irAEs are frequent, often severe and can result in morbidity and rarely death. Very little is known about how irAEs develop.

Aims: To investigate immune mechanisms that underlie irAE and to determine why only some patients are affected by it.

Methods: Deep immune phenotyping using mass cytometry (CyToF) was performed on peripheral blood mononuclear cells taken from patients who received combination immunotherapy (ipilimumab and nivolumab or pembrolizumab) and developed colitis (n=19). Samples from patients who received combination immunotherapy and never developed any signs of colitis (n=18) were used as control for comparison. Samples were taken both at baseline (prior to immunotherapy) and during toxicity. Multiplex immunohistochemistry was performed on colon biopsy samples from patients with colitis (n=26), including some paired samples with matching PBMCs.

Results:.Patients who developed colitis during immunotherapy had multiple myeloid populations that were significantly different at baseline, including subsets of monocytes. There were changes in the systemic immune populations during immunotherapy, including a significant increase in some T cell populations in patients who developed colitis compared to those who did not. Monocytic infiltration of the colonic mucosa was seen even in non-inflamed regions, suggesting that this could preceed inflammatory lesions. Inflamed regions of the colonic mucosa were characterised by an expansion of tissue-resident CD8+ T cells and CD16+ myeloid cells.

Conclusion: Infiltration of systemic myeloid cells and local expansion of T cells are likely drivers of colitis in patients receiving combination immunotherapy**.** Systemic innate immune makeup is also likely to predispose some patients to colitis and therefore this could also predict the development of irAEs.

Paper ID 126

Moral distress among oncology and palliative care HCPs in Australia: A qualitative study.

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Background: Cancer and palliative care are complex and can involve challenging and distressing clinical decisions. When these decisions conflict with health care professionals' (HCPs) values they may experience moral distress. Moral distress is correlated with increased burnout and lower workforce retention.

Aim: This study aimed to qualitatively explore experiences of moral distress among HCPs within oncology and palliative care in Australia to inform how to best address moral distress among this group.

Methods: Qualitative interviews with 33 oncology and palliative care HCPs explored participants' experiences of moral distress. Thematic analysis using a Framework Approach identified morally distressing situations and the impact on the individual, their teams, and the organisation. Strategies used to manage moral distress were explored.

Results: Thematic analysis revealed six themes: (1) values and their conflicts, (2) moral distress and interactions between people, (3) moral distress and systematic factors, (4) moral distress within oneself, (5) preventing and managing moral distress, and (6) the impact of moral distress. At the core of HCPs experiences of moral distress were patient- and care-centred values and the violation of the oath to ''Do No Harm''. Moral distress was perceived to be covert and primarily arose in response to day-to-day dilemmas. Moral distress was predominantly related with interactions between people and structural factors. Differences in experiences emerged across disciplines and career stage. Moral distress impacted individuals, relationships, clinical care, and policy. Strategies, effective and not, for managing moral dilemmas and distress were highlighted, as well as perceived barriers to dealing with moral distress.

Conclusions: The impact of moral distress on individual wellbeing and workplace tenor within oncology and palliative care highlight the need for interventions to identify and manage morally distressing situations. Interventions are needed for organisations and systems to support HCPs to provide optimal care while ensuring workforce retention, health, and functioning.

Paper ID 146

Targeting Mitochondrial Dynamics to Prevent Drug Induced Cancer Stem Cells & MDR in Glioblastoma

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Background: Less than 5% of glioblastoma (GBM) patients survive 5-years following diagnosis. GBM are heterogeneous tumours composed of a small population of glioma stem cells (GSCs), which exhibits high tumorigenicity. GSCs are linked to recurrence and drug-resistance, which are a hallmark of highly aggressive drug-resistant brain cancers. GBM patients' are currently treated with the Stupp protocol, which includes surgical resection, followed by radiation and temozolomide (TMZ). As the administration of chemotherapeutics/radiation occurs in cycles to allow patient recovery, this also provides an opportunity for regrowth of drug-resistant tumours and the phenotypic shift of non-GSCs to GSCs. Currently, no clinical treatments are available for eradicating GSCs.

Aim: Our aim was to examine whether the FDA-approved antibiotic and mitochondrial targeting doxycycline (DXC), can be repurposed as an adjuvant-therapy for GBM along with conventional drugs such as TMZ to eradicate GSCs in GBM.

Methods: This study utilized GBM cell lines, U87MG-Parental and U87MG-TR (Temozolomide-Resistant) cells to elucidate the mechanism of DXC in GSCs. Cell lines were treated with known brain penetrant drugs of different range/target action: (i) commonly used chemotherapeutics (temozolomide), (ii) mitochondrial biogenesis-inhibitor, DXC, and (iii) mitochondria fission targeting drugs (mdivi-1) as single/combination-treatment. Expression of GSCs/resistance/signaling markers was measured by western blotting. Drug-resistance and stemness-phenotype GSCs regrowth was determined by neurosphere-formation (Elispot); and mitochondria turnover/mass and activity was determined by staining with mitochondrial markers (VDAC/TOM20) and measured by fluorescence microscopy and flow cytometry.

Results: Our preliminary studies demonstrated that DXC significantly decreases CSCs markers and decrease regrowth of GBM neurospheres. DXC was also found to re-sensitize and shift resistant U87MG-TR cells with a CSCs phenotype to a non-CSCs phenotype that is more sensitive to TMZ treatment.

Conclusion and Translational potential: Repurposing existing FDA-approved drugs, such as DXC, show potential to be fast-tracked as combinational/adjuvant therapy with TMZ for patients with recurrent and resistant-GSCs.

Paper ID 153

Patient experiences of melanoma self-surveillance using mobile digital technology.

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Background: Melanoma surveillance can require frequent visits to a hospital clinic, with associated travel, cost and time burden. It is unknown whether mobile digital technology along with remote communication with healthcare providers could facilitate self-surveillance at home.

Aim: This study aimed to explore patients' experiences of using a mobile dermatoscope (magnifying camera device that attaches to a smartphone) and accompanying app for tracking and sending images, to gain understanding of the acceptability of such technologies and remote care delivery.

Methods: Semi-structured interviews and theoretically driven thematic analysis utilising the extended Technology Acceptance Model (TAM) framework. This qualitative study was nested within a pilot randomised controlled trial (RCT), conducted at melanoma centres in NSW.

Results: A total of 20 participants (8 women and 12 men; median age 62) were interviewed. Participants saw benefit in the intervention due to increased access to care, enhancement of early detection and increased awareness of their skin and importance of skin self-examination (SSE). Previous experience with technology increased ease of use while learning how to use the intervention tools. Effective help from a skin check partner and assistance from clinic staff increased ease of use during the follow up period, while low intervention self-efficacy, having many moles and technical problems decreased ease of use and usefulness. Competing commitments and not having a willing or available skin check partner were barries to using the intervention.

Conclusions: Melanoma patients are receptive to and see benefit in using mobile teledermoscopy tools and remote care as part of patient-led surveillance, in addition to usual care. However, learning to use the tools with confidence requires practice; and patients and their skin check partner require educational and technical support, particularly if they have many moles or low technology self-efficacy. Addressing these barriers will facilitate translation into clinical practice.

Paper ID 158

CMA mediates the ARPI stress response in prostate cancer, promoting ARPI treatment resistance

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Prostate cancer (PCa) is the second leading cause of cancer related death in men worldwide, with androgen deprivation therapy (ADT) and androgen receptor pathway inhibition (ARPI) the standard of care for advanced PCa. ARPI subjects PCa cells to acute metabolic stress through reduced biosynthesis and energy production, leading to the upregulation of acute stress mechanism that promote treatment resistance. Using mass spectrometry to profile proteomic pathway alterations associated with the ARPI stress response, we identified the upregulation of chaperone mediated autophagy (CMA), supported by the increased expression of the lysosomal associated membrane protein 2a (L2A) and CMA active lysosomes. CMA is a selective protein degradation pathway that specifically targets protein substrates via a CMA recognition motif. While yet to be defined in PCa, CMA is a stress response mechanism induced by various stress conditions, such as genotoxic, proteotoxic, oxidative stress and an essential survival mechanism in cancer cells during energy depleted metabolic stress. Preliminary data illustrates the importance of CMA in PCa and the ARPI stress response, by preventing PCa cell proliferation following CMA inhibition, which is further enhanced by Enzalutamide. CMA inhibition also leads to the downregulation of mTORC1 signaling and promotes chromatin silencing. Furthermore, the overexpression of L2A also promotes PCa cell proliferation during Enzalutamide treatment, with RNA-seq data showing an upregulation of hallmark target genes of AR-indifferent PCa growth. In summary, our preliminary data illustrates the importance of CMA in mediating the ARPI stress response in PCa, providing novel insights into the mechanisms of ARPI treatment resistance.

Sydney Cancer Conference 2021

ABSTRACTS:

POSTER PRESENTATIONS WITH MINI-ORALS

ABSTRACTS FOR POSTER PRESENTATIONS (with mini-oral)

Paper ID 5

Testing the threat interpretation model of fear of cancer recurrence in women with breast cancer

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Objective: The Cancer Threat Interpretation model proposes that severe levels of fear of cancer recurrence/progression (FCR/P) occur when people misinterpret ambiguous physical symptoms as a sign of recurrence. However, this assertion has not been tested. The primary aim of this research was to test whether interpretation biases moderate the relationship between symptom burden and FCR/P in women with breast cancer, as the theory predicts.

Method: One hundred and forty-seven women with breast cancer volunteered and completed an questionnaire, including demographic and medical information and measures on fear of cancer recurrence (FCR), fear of progression (FOP), interpretation bias, symptom and burden. Other known predictors of FCR/P were also assessed, including metacognitions, bodily threat monitoring and threat appraisal.

Results: Women with clinically significant levels of FCR/P were more likely to interpret ambiguous words as health-related and carried a higher symptom burden than women with levels of FCR/P in the normal range. As expected, those with clinically significant levels of FCR/P also reported more unhelpful metacognitions, symptom monitoring and threat appraisal as compared to women with lower levels. FCR was associated with both symptom burden ($r = .40$, $p < .001$) and interpretation bias ($r = .45$, $p < .001$). Interpretation biasand symptom burden ($r = .31$, $p < .001$) were also associated. Importantly, moderation analyses confirmed that interpretation bias moderated the relationship between symptom burden and FCR. However, this was not the case with FoP ($F(1, 143) = 0.21$; $p = .65$).

Conclusion: We found that women with breast cancer with clinically significant levels of FCR/P interpreted ambiguous words as health-related more often and experienced more symptoms than than those with lower levels of FCR/P. Moreover, we found that interpretation bias moderated the relationship between symptom burden and FCR/P. That is, symptom burden predicted FCR/P more amongst those with higher levels of interpretation bias, as the threat interpretation model predicts.

Paper ID 6

Cancer patient experience of uncertainty while waiting for genome sequencing results

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Background: There is limited knowledge about cancer patients' experiences of uncertainty while waiting for genome sequencing (GS) results, and whether prolonged uncertainty contributes to poorer psychological outcomes.

Aims: Investigate uncertainty in patients with a cancer of likely hereditary origin while waiting for GS results.

Methods: We collected questionnaire and interview data at baseline, and at three and 12 month follow up (prior to receiving results).

Results: Participants (N=353) had negative attitudes towards uncertainty (M=4.03, SD 0.68) at baseline, and low levels of uncertainty at three (M=8.23, SD 7.37) and 12 months (M=7.95, SD 7.64). Greater perceived susceptibility for cancer (r(348)=.14, p<.01), fear of cancer recurrence (r(348)=.19, p<.01), perceived importance of GS (r(350)=.24, p<.01), intention to change behavior if a gene variant found (r(349)=.29, p<.01), perceived ability to cope with results (r(349)=.36, p<.01), and satisfaction with decision to have GS (r(350)=.52, p<.01) were significantly correlated with negative attitudes towards uncertainty at baseline. Lower perceived ability to cope with results (B=-.1.881 [-3.403, -.359], p=.016) at baseline, greater anxiety about GS (B=.347 [.148, .546], p=.0012) at three months, and greater perceived uncertainty about GS (B=.494 [.267, .721] p=.000) at three months predicted greater perceived uncertainty about GS at 12 months. Greater perceived uncertainty about GS at three months predicted greater anxiety about GS at 12 months (B=.291 [.072, .509], p=.009). Semi-structured interviews revealed that while participants were motivated to pursue GS as a strategy to reduce their illness and risk uncertainty, GS generated additional uncertainties. Some uncertainties and coping strategies were consistently discussed over the 12 months, while others emerged over time.

Conclusions: This study demonstrates the complexity of uncertainty generated by GS for cancer patients and provides further support for the inter-relationship between uncertainty and anxiety. Helping patients manage their uncertainty may ameliorate psychological morbidity.

Paper ID 7

PanCan Diagnosed: The Early Diagnosis and Personalized Treatment of Pancreatic Cancer

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miRNAs have shown to be significant in the development of cancer tumors. Currently, pancreatic cancer's (PC's) early diagnostic rate is just 9% as screening methods are unattainable, making it the fourth leading cause of cancer death. Many studies have achieved low accuracy (70-75%) as they use methods that do not take into account the 33% misdiagnosis rate of PC with other cancers. As a result, feature selection, ensemble algorithms, and interpretability techniques were used to find significant miRNAs in order to construct an early diagnostic tool for PC. In the first phase, recursive feature elimination algorithms were used to find 200 differentially expressed miRNAs in PC and no PC samples as well as early and late PC samples. In the second phase, an ensemble algorithm was constructed out of K-Nearest Neighbor, Naive Bayes, Neural Network, and Logistic Regression models in order to diagnose PC and distinguish between early and late stages. In the third phase, XGBoost, SHAP, and Skater interpretability methods were used to find which miRNAs were significant in model predictions. In the fourth phase, a user interface, PanCan Diagnosis, was designed to test if a person had no, early, or late stage PC and also displayed the patient's most differentially expressed miRNAs. This novel tool is the first in literature to receive a PC diagnostic accuracy of above 90%, seek miRNAs that can lead to personalized treatment of early and late stage PC samples, offers a ten-fold improvement in monetary costs, and is two times faster than current methods.

Paper ID 11

Inhibiting the interaction of human secreted phospholipase IIA and vimentin in prostate cancer.

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Background: Prostate cancer (PCa) causes 3500 deaths in Australia per year, highlighting the need for drug development targeting novel pathways. Our orally-active non-toxic cyclic peptide inhibitor, c2 is derived from the inflammatory protein secreted phospholipase A_2, (hGIIA). hGIIA is aberrantly expressed in prostate tumours, causes proliferation in PCa cell lines and its expression correlates with disease severity. c2 treatment inhibits proliferation, reducing xenograft tumour volume. We hypothesise that hGIIA stimulates eicosanoid production through binding to vimentin, a cytoskeletal protein up-regulated in PCa and that c2 inhibits this interaction.

Aim: To examine the hGIIA/vimentin interaction in PCa cells, and how c2 affects this interaction.

Methods: hGIIA expression and vimentin colocalization was observed *via* immunofluorescence imaging of three PCa cell lines (PC-3, LNCaP and DU145). Co-immunoprecipitation and FLIM-FRET analysis confirmed binding *in vivo*. Enzyme immunoassay (EIA) confirmed binding *in vitro*. Live cell imaging documented interactions between hGIIA and vimentin, as well as cell entry, localisation and effect of c2.

Results: Both endogenous hGIIA and c2 alone localise within caveolae, colocalising with vimentin in PC-3 and LNCaP. hGIIA and vimentin directly bind in these cell lines, with EIA showing selective hGIIA binding to coil 2 of vimentin. Vimentin mediates intracellular trafficking of hGIIA and c2 inhibits hGIIA entry. EIA assays confirm c2 inhibits the hGIIA/vimentin interaction by also binding to coil two, confirming c2's role as a 'vimentin blocker'.

Conclusion: hGIIA and vimentin bind *in vivo* in PCa cells indicating a possible scaffolding role for vimentin, linking inflammation and tumorigenesis in PCa. c2 is cell permeable and blocks interactions with hGIIA and vimentin *in vitro*, and colocalises with hGIIA *in vivo*. Thus, c2's anti-cancer properties are through inhibiting this interaction. This is crucial information for the progression of c2 to further clinical trials, and the development of new drugs targeting inflammation-driven advanced PCa.

Paper ID 12

Using Aboriginal governance and engagement to support cancer research

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Aboriginal leadership and engagement are critical to achieving meaningful and lasting improvements in cancer outcomes for Aboriginal people. The NSW Aboriginal Cancer Governance and Engagement Framework (the Framework) supports the Cancer Institute NSW (the Institute) to implement a collaborative approach to developing research initiatives to improve cancer outcomes for Aboriginal people in NSW.

The Framework has been designed, refined and agreed in partnership with the Aboriginal Health and Medical Research Council and Aboriginal key stakeholders and developed within a context of evolving decision making in relation to:

- the overarching state-wide governance of the NSW Cancer Plan
- an optimal approach to informing and coordinating a state-wide approach to achieve the goals of the NSW Cancer Plan for Aboriginal communities in NSW.

The establishment of a governance framework that has Aboriginal leadership is a key step in ensuring that decision making in Aboriginal cancer control is culturally safe and improves cancer outcomes for Aboriginal people. Across the Institute, a core governance consideration is to aim for majority Aboriginal representation on committees that focus on determining priorities and initiatives for Aboriginal people and communities.

The framework has been pivotal in ensuring Aboriginal leadership, participation and co-design in Aboriginal research activities. The Institute's Aboriginal Cancer Advisory Group (ACAG) plays a key role in ensuring that Aboriginal Community Controlled Health Services and Aboriginal Health Workers, working in Local Health Districts and Primary Health Networks, contribute to the development and implementation of research and other projects.

Aboriginal Elders and community members on the ACAG are reimbursed, in acknowledgement of their cultural knowledge and experience, and it ensures that there is direct community input. Members of the ACAG are also allocated to research and improvement projects of interest or expertise, where they are formally acknowledged for their contribution and listed as co-authors on these studies.

Examples of ACAG involvement in research activities to date are:

- Aboriginal Smoking Scoping Project
- WNSW Aboriginal Cancer Patterns of Care Project
- CanDLe Project
- Portal development - Aboriginal and Torres Strait Islander status of cancer clinical trial participants.

Paper ID 14

DPP9: Comprehensive In Silico Analyses of LoF Variants and Associated Gene Signatures in HCC

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Background: Dipeptidyl peptidase (DPP) 9, DPP8, DPP4 and fibroblast activation protein (FAP) are the four enzymatically active members of the S9b protease family. Associations of DPP9 or DPP8 with human liver cancer have not been examined. Genome-wide association studies have found that intronic single nucleotide polymorphisms (SNPs) in *DPP9* are associated with severe COVID-19 and lung fibrosis. However, exonic SNPs in *DPP9* and *DPP9* loss of function (LoF) variants have not been explored.

Methods: Large-scale human genetic databases including The Cancer Genome Atlas (TCGA) were interrogated.

Results: We found that *DPP8* and *DPP9* are intolerant to LoF variants, which suggests that these enzymes, but not *DPP4* and *FAP,* are crucial for life in humans. Uterine corpus endometrial carcinoma (UCEC) was the most commonly diagnosed cancer in patients with *DPP9* LoF variants, and low *DPP9* expression was associated with poor survival in UCEC. The two DPP9 intronic SNPs that have been associated with lung fibrosis and COVID-19 were not associated with liver fibrosis or cancer. All four enzymes were overexpressed in liver tumours. Increased *DPP9* expression was associated with extreme obesity in HCC patients. There was no association between *DPP9* expression intensity and HCC survival. However, high expression of all four *DPP4*-like genes was significantly associated with poor survival in HCC. Moreover, high expression of genes that positively correlated with overexpression of *DPP4*, *DPP8*, and *DPP9* was associated with very poor survival in HCC. Enriched pathways analysis of these in-common correlated genes featured Toll-like receptor (TLR) and SUMOylation pathways.

Conclusion: This comprehensive data mining suggests that DPP9 is crucial for human survival and the DPP4 protease family is important in cancer pathogenesis.

Paper ID 16

Dipeptidyl Peptidase Inhibition Enhances CD8 T cells and Inflammasome in Hepatocellular Carcinoma

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Background: We recently found that mRNA expression of the Dipeptidyl Peptidase 4 (DPP4) gene family is highly upregulated in human hepatocellular carcinoma (HCC), and is associated with poor survival in HCC patients. Compounds that inhibit all four enzymes of the DPP4 family, such as Talabostat, can mediate tumour regression by immune-mediated mechanisms. DPP4 inhibition increases CXCR3 signalling while DPP9 inhibition increases NLRP1 inflammasome activation, so these are potential mechanisms in HCC.

Aim: This study aimed to understand the DPP4 enzyme family in the development of HCC and to evaluate effects of a pan-DPP inhibitor (ARI-4175) in early HCC in mice.

Methods: We have developed a novel primary HCC model that recapitulates modern human HCC. Male mice received diethylnitrosamine when 12 days old, then from weaning ate an atherogenic diet and drank thioacetamide (200 mg/L) until 28 weeks of age (endpoint). At 16 weeks of age, ARI-4175 at 6 mg/kg body weight was injected subcutaneously daily for 6 weeks. DPPs were quantified by qPCR and by enzyme assays.

Results: This is the first report on intrahepatic mRNA expression and intrahepatic and plasma peptidase activity of the DPP4 enzyme family in HCC-bearing mice. We demonstrated inhibition of the DPP4 enzyme family by ARI-4175 and lowered numbers of macroscopic liver nodules in such mice. In addition, ARI-4175 increased intrahepatic inflammatory cell infiltration, including $CD8^+$ T cell numbers, into the HCC-bearing livers. Furthermore, ARI-4175 activated a critical component of the inflammasome pathway, caspase-1, in these HCC-bearing livers. This is the first evidence of caspase-1 activation by a pan-DPP inhibitor in liver.

Conclusions: Our data suggest that targeting the DPP4 enzyme family may be a novel and effective approach to promote anti-tumour immunity in HCC.

Paper ID 17

A systematic review and meta-analysis of smoking behaviour changes during the COVID-19 pandemic.

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Background: Globally, tobacco smoking remains the single largest cause of premature death, yet its prevalence remains high. The COVID-19 pandemic has forced nations to take unprecedented measures including 'lockdowns' that might impact tobacco smoking behaviour.

Aim: We performed a systematic review and meta-analyses to assess smoking behaviour changes during the early phases of the COVID-19 pandemic.

Methods: We searched Medline, Embase, PsycINFO, BioRxiv, MedRxiv, and SSRN databases (January-November 2020) for published and pre-print articles that reported specific smoking behaviour changes or intentions after the onset of the COVID-19 pandemic. We used inverse variance random-effects models to pool prevalence ratios comparing the prevalence of smokers during and before the COVID-19 pandemic, and the prevalence of increased, decreased, uptake of, cessation of, attempts to quit and intention to quit smoking during compared to before the pandemic.

Results: We identified 33 articles that met our inclusion criteria (29 cross-sectional and 4 before-and-after studies) across 22 countries, with a total of >146,000 participants. Smoking prevalence was slightly reduced during the pandemic, with a pooled prevalence ratio of 0.91 (95%CI: 0.84-0.99). In studies limited to smokers (n=21), 30% (95%CI: 22-40%) smoked more, 17% (95%CI: 12-23%) smoked less, and 27% (95%CI: 4-60%) reported quitting smoking, respectively. Among non-smoking participants, 4% (95%CI: 1-9%) started smoking during the pandemic. However, all studies were considered to be at high risk of bias due to use of non-representative samples, likely non-response bias, and utilisation of non-validated questions.

Conclusions: Smoking behaviour changes during early phases of the COVID-19 pandemic were highly heterogeneous. Meta-analyses indicated slightly lower overall smoking prevalence during the pandemic, but higher smoking intensity among smokers. Updates of this review are planned to assess longer term changes during the pandemic and consolidate high-quality evidence from representative surveys.

Paper ID 18

Cost analysis of breast cancer chemotherapy drugs in Australia.

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Background: In Australia, the number of breast cancer patients is increasing with over 20,000 cases reported in 2020. Chemotherapy drugs are a significant contributor to the financial costs of treatment, as their use is generally concomitant and expensive.

Aim: The aim of this longitudinal study is to evaluate the cost of chemotherapy drugs and protocols over time from 2018 to underline the importance of preventative programs.

Methods: Chemotherapy protocols and breast cancer drugs used in Australia were identified using the Australian EVIQ database**.** Drug costs were calculated using the Pharmaceutical Benefits Scheme (PBS) website using the dispensed price for maximum amount price. The total number of prescriptions dispensed for each drug and the repartition of private to public prescriptions in each state were calculated based on the Australia Medicare reports.

Results: In 2018, there were 31 drugs used for the treatment of breast cancer, all of which were listed on the PBS, except for fulvestrant. The cost of the drugs and each treatment protocol ranged from $0.0014/mg to $280.04/mg and $109.20 to $41,543.22, respectively. The most expensive drugs, trastuzumab and pertuzumab, were prescribed 12-fold fewer times than the least expensive drugs, anastrozole and tamoxifen. However, these high cost drugs were part of the most expensive chemotherapy protocols in all of the adjuvant ($30,498/round), neoadjuvant ($22,600.26/round) and metastatic ($41,543.22/round) breast cancer protocols. Additionally, cost was found to be specifically problematic in NSW due to the high frequency of private prescriptions compared with public prescriptions.

Conclusions: Breast cancer chemotherapy drugs are very costly for patients and the Australian government. Some drugs are expected to come off patent within the incoming years, but new drugs will also enter the market. Therefore, preventative programs may be a cost-effective way to reduce treatment costs.

Paper ID 19

Mortality review: Timing of Goals of care(GOC) discussions in tertiary oncology inpatients

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Background: Measures of End of life quality improve with earlier (>30days before death) GOC discussions. Unplanned hospitalisation predicts poor survival in advanced cancer patients however GOC discussions occur late.

Aim: to assess timing and events of GOC discussion in oncology inpatient mortality cases over 12 months at our tertiary centre.

Methods: Electronic medical records review of inpatient Mortality cases between April 2019-2020. Assess timing of GOC discussions: days prior to date of death(DOD), days since admission, by whom, events triggering discussion, medically driven vs shared decision making.

Results: 86 patients. 82 GOC completed at time of death. 10 had GOC prior to admission, 14 completed day of oncology admission. Majority completed reactive to clinical deterioration: number of days prior to death Mean 6.41, median 3, range 0-154(Figure1). More than half GOC discussions during final 3 days of life. 74 discussed as shared decision making. 27 by oncology consultant, 20 senior oncology registrar. Majority by junior JMO, relieving or other specialty doctor.

Conclusion: Despite evidence for improved patient outcomes with earlier GOC these are not done early when patients are well but instead are reactive to deterioration and often not completed by senior oncology staff. We plan to intervene to increase rates of earlier GOC discussion then re-audit our service.

Paper ID 20

Targeted Metabolomic Profiling of Cancer Cell Lines of Varying Origins

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Background: Cancer cells have distinctive metabolic features that allow increased biomass production to support autonomous expansion. It is now clear that metabolic heterogeneity exists between and within cancer types, between low grade and high-grade disease, and between primary tumours and metastatic tissue. The present study takes a pan-cancer approach to identify metabolomic-based signatures that can form the basis for subsequent testing of novel therapeutic targets for prostate and other cancer types.

Aim: Identify metabolic subtypes in a range of diverse range of cancer cells from varying origins

Methods: A broad range of cell lines (cancer and non-cancer) of varying origins were used: Prostate (n=12), Breast (n=7), Liver (n=6), Endometrial (n=9), Glioblastoma (n=2), Pancreatic (n=5), Ovarian (n=3), Melanoma (n=4), Lung (n=3), Head and neck (n=2), and Colorectal (n=4). Cultured cells were extracted for high-resolution metabolomic analyses that were performed at Sydney Mass Spectrometry.

Results and Conclusions: There was no identifiable clustering of our results that were driven by cancer cell origin, culturing conditions, or common mutations in molecular drivers of cancers, including P53, PTEN, BRAF, and NRAS. Using K-means clustering with Pearson correlation as the distance metric, we identified 7 unique clusters that consisted of a heterogenous mix of cell lines of different origins. For example, one heterogeneous cluster was enriched for TCA cycle metabolites, while another was enriched for glutamine related metabolites. The early outcomes of this study provide proof-of-concept evidence and that there is potential for therapeutically targeting metabolic pathways that are exhibited across different subtypes of cancers of different origins.

Paper ID 21

Prevalence of unmet needs in Indian Head & Neck Cancer patients

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Aims: 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.

Paper ID 22

Registry Automated Data Extraction Evaluation – Findings from NSW Cancer Registry

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Background: The New South Wales Cancer Registry (NSWCR) is a population-based cancer registry (PBCR). Cancer notifications come from external sources (e.g. hospitals and pathology laboratories) and are processed by medical coders. In 2017, NSWCR implemented the Abrevio software, which uses machine-learning algorithms to perform automated data extraction from pathology reports.

Aim: to evaluate Abrevio's auto-extracting capabilities, and ultimately improve the accuracy of auto-extraction.

Methods: To inform the evaluation approach and understand the use of artificial intelligence (AI) in cancer registries, a literature review was conducted and representatives from other Australasian PBCRs were consulted. The evaluation was separated into three scenarios: prostate cancer, triple negative breast cancer and colorectal cancer, and 325 pathology reports were analysed in each scenario. Examples of data items evaluated included:

- Prostate cancer: Specimen Type, Gleason score, TNM stage;
- Breast cancer: HER2 status, PR status and ER status;
- Colorectal cancer: Grade, MLH-1, MSH-2 and MSH-6.

Data were manually extracted and auto-extracted. For each data item, percentage agreement scores between manual and automatic extractions were calculated. Discrepancies were examined to investigate why auto-extractions failed, and a list of recommendations and action points were developed.

Results and conclusions: Based on agreement scores, data items were grouped into three categories: 1) high accuracy (>90%), 2) reasonably high accuracy (between 75% and 89%, inclusive) and 3) low accuracy (below 75%). Where Abrevio extracted a value, the value was usually correct. Failure to auto-extraction was mainly due to 1) Abrevio not being able to detect a value and/or 2) Abrevio could not consolidate multiple values to a single value. It was decided that auto-extractions be brought into the NSWCR for data items with high accuracy and reasonably high accuracy. Feedback to improve Abrevio's AI engine was provided to the developers, and the use of standardised vocabulary/formatting was encouraged among pathologists.

Paper ID 23

Development of Novel Autophagy Inhibitors Based Anti-Cancer Combination Therapy

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

Aim: Assessment the efficacy of autophagic inhibitors in combination with standard chemotherapeutics.

Methods: Triple negative breast cancer and oral cancer cell lines were used in this study. Levels of autophagic marker, LC3-II, were determined by immunoblotting under different microenvironmental stressors. We also utilized autophagy inhibitors inhibiting two major regulatory complexes (*i.e.,* ULK-1 and Beclin-1 complexes) in the core autophagic machinery. IC_{50} of the inhibitors was determined using cellular proliferation assay. The synergy between different autophagy inhibitors, and also, between autophagy inhibitors and standard chemotherapeutics (*e.g.,* Paclitaxel) was determined using Chou-Talalay method.

Results: Increased autophagy induction was observed after incubation of cells under microenvironmental stressors in all cell lines. On the other hand, there was marked decrease in IC_{50} of autophagy inhibitors (Spautin-1, MRT68921 and SAR405) after incubation under microenvironmental stressors. Notably, Beclin-1 complex inhibitor (*i.e.,* SAR405) and ULK-1 complex inhibitor (*i.e.,* MRT68921) demonstrated potent synergism (Combination Index (CI) < 1.0) in their anti-proliferative activity. Synergism was also observed between autophagy inhibitors and chemotherapeutics. Moreover, Beclin-1 inhibitors also showed synergism with ULK-1 inhibitors after incubation of cells with microenvironmental stressors.

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

Paper ID 24

Mechanism analysis of malignant suppression of cancer by Bowman-Birk protease inhibitor (BBI)

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Background: In recent years, there has been tendency for dogs to have longer lifespans. Therefore, the increasing prevalence of cancers has become severe problem to expand life expectancy. A cancer that has been reported to have an increased risk of morbidity with aging is a malignant tumor derived from melanocytes called melanoma. It is known that malignant tumors derived from melanocytes occur very frequently in dogs, and 70% of them have been diagnosed as melanoma. Furthermore, melanoma also acquires resistance for chemotherapeutic agents within a few months, so the screening of effective anti-melanoma agents is absolutely required for the establishment of a new anti-melanoma therapy. BBI contained in soybeans has high bioavailability and exerts a tumor-suppressing effect. Previous studies have shown that BBI reduces malignant phenotypes of the melanoma via increasing the expression of It is difficult to completely cure melanoma due to highly frequent metastasis, and has a significantly poor prognosis. a tumor suppressor gene, connexin 43 (cx43). However, the mechanism of action of BBI to suppress cancer via Cx43 has not been proven in dogs. Therefore, the purpose of this study was to analyze the mechanism of suppression of cancer malignant transformation mediated by Cx43 induction by BBI in canine cell lines.

Methods: Canine oral melanoma cells (TLM-1) were used. The cells were treated with BBI. We evaluated cell viability and protein expression levels.

Results: BBI treatment reduced cell viability. In addition, a significant increase in Cx43 protein expression was confirmed. In addition, it was suggested that the expression of proteins related to epithelial-mesenchymal transition (EMT) was suppressed.

Conclusions: From this study, it seems to be possible that BBI acta as an effective agent to suppress canine melanoma growth, in part due to the induction of Cx43. In addition, since the tendency to suppress EMT was confirmed, metastasis may be suppressed. We are currently investigating whether induction of Cx43 relies on gap junctions to exert a tumor-suppressive effect.

Paper ID 26

Patient preferences in prostate cancer care: a review of discrete choice experiments

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Background: Discrete choice experiments (DCEs) are an increasingly popular quantitative method to elicit patient preferences for their healthcare. While systematic reviews of preferences in some cancer types or treatment modalities have been conducted, an exploration of DCEs in prostate cancer, the fourth most common cancer worldwide, is overdue.

Aim: This systematic review aims to describe prostate cancer-related DCEs and identify gaps and directions for future research.

Methods: We located DCEs related to prostate cancer from four seminal systematic reviews of DCEs in healthcare, covering a period from 1990-2017. Data was extracted on study characteristics and methods, and study quality assessed using a validated checklist. Emergent themes, gaps and opportunities for future research were identified.

Results: 633 cancer-related DCEs were identified, with 9 related to prostate cancer. The prostate cancer DCEs explored preferences for treatment (*n*=6), screening (*n*=2), and survivorship care (*n*=1). DCEs were concentrated in patient or survivor cohorts, although study characteristics and findings varied significantly across the sample. Patients considering treatment valued survival and costs but were prepared to trade off survival for reduced likelihood of bone complications and malaise. The attributes that influenced screening decisions in both studies included avoidance of prostate cancer deaths, likelihood of biopsy, and cost. Prostate cancer survivors, though under-studied, valued continuity of care, face to face support, and dietary advice.

Conclusions: Prostate cancer patient preferences are heterogenous but there is evidence that they are willing to trade between aspects of their health and care in the context of treatment, screening and survivorship. This is one of the few cancers where patients report preferences for reduced side effects and improved quality of life over survival, and thus warrants further investigation. Several important gaps in knowledge around patient preferences for prostate cancer care remain, with scope for future DCEs to inform patient-centred care.

Paper ID 27

Cardiac assessment in Australian patients receiving trastuzumab for HER2+ early breast cancer

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Background: Regular cardiac function assessment is recommended for patients with HER2-positive early breast cancer (HER2+EBC) for timely detection and management of trastuzumab-associated cardiotoxicity.

Aim: To examine the rates and predictors of cardiac assessment among patients receiving trastuzumab for HER2+EBC.

Methods: We conducted a population-based cohort study of Australians initiating Pharmaceutical Benefits Scheme-funded (neo)adjuvant trastuzumab for HER2+EBC between 1/1/2015 and 15/4/2019. We used Medicare Benefit Schedule claims to identify patients receiving government-subsidised echocardiograms and multi-gated acquisition scans. We determined the number of patients receiving guideline-recommended assessment, defined as a baseline cardiac assessment (between 120 days before and 30 days after trastuzumab initiation) plus regular on-treatment cardiac assessments (at least every 120 days). We used logistic regression to examine factors associated with guideline-recommended assessment.

Results: Our cohort includes 5621 patients (median age 56 years), of whom 4984 (88.7%) had a baseline cardiac function test. Echocardiograms constituted the majority of baseline (71.1%) and on-treatment (76.1%) cardiac function tests. Among 4280 patients with ≥12 months of follow-up, 2702 (63.1%) had guideline-recommended cardiac assessment. Rates of guideline-recommended assessment increased over time (60.9% in 2015 vs 68.3% in 2018, OR 1.34, 95% CI 1.06-1.69). The proportion of patients receiving guideline-recommended cardiac assessment varied by State/Territory (range 39.3-68.7%) and remoteness (range 61.8-69.8%). Patients with ≥4 baseline comorbidities were less likely to have guideline-recommended cardiac assessment than those with 0-1 comorbidities (OR 0.79, 95% CI 0.65-0.97). There was no association between baseline cardiac risk or anthracycline use and the likelihood of receiving guideline-recommended cardiac assessment.

Conclusions: The majority of patients receiving (neo)adjuvant trastuzumab had guideline-recommended cardiac assessment. Variations in cardiac assessment predominantly related to system-level factors, such as year of diagnosis and geography, rather than individual patient factors. Investigation into system-level barriers to cardiac monitoring may help improve rates of guideline-recommended cardiac assessment in patients with HER2+EBC.

Paper ID 28

NK cells preferentially target prostate cancer stem-like cells

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Background: Cancer stem cells possessing high tumorigenicity are involved in the development of cancer and subsequent infiltration / metastasis. In recent years, the formation of cancer stem cells in tumor tissues is considered as the first step in carcinogenesis. Therefore, direct elimination of cancer stem cells is thought to lead to primary, secondary and third prevention of cancer, but the effective approach has not yet been established. Thus, we focused on NK cells playing central roles of nature immunity. It has been reported that NK cells directly attack cancer cells and virus-infected cells without pre-sensitization, and the higher the activity, the lower the risk of developing cancer. Until now, it has not been clarified why this phenomenon occurs. On the other hand, we hypothesized that the cancer stem cell targeting mechanism of NK cells might be involved. In this study, we focused on prostate cancer, which is more easily infiltrated by NK cells of various tissues, and estimated the effect of NK cells on prostate cancer stem cells.

Method: Prostate cancer stem-like cells (LN-stem) were concentrated from the androgen-dependent human prostate cancer cells (LNCaP: LN) by a three-dimensional culture method. LN and LN-stem were co-cultured with human NK-like cells (KHYG-1), respectively, KHYG-1 cells were removed and then cell viability was measured by WST-8. In addition, gene expression analysis and FACS analysis were performed to identify the NK cells-mediated cytotoxic signal pathway.

Results: KHYG-1 injured LN-stem more severely than LN. However, the protein levels on the activating ligands involved in degranulation had no differences between LN and LN-stem. On the other hand, the gene expression and cell surface expression of DR5, which is a receptor for the death receptor pathway, in LN-stem, was higher than that in LN.

Discussion: This study revealed that prostate cancer stem-like cells were more susceptible to NK cell attack than parental prostate cancer cells. In addition, it was suggested that the death receptor pathway starting from DR5 is involved in this phenomenon.

Paper ID 29

Investigating and addressing clinical variation in lung cancer - analysis from the EnRICH Program

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Background: Lung cancer is the leading cause of cancer-related death, morbidity, and burden of disease across Australia. There is an urgent need to identify and reduce unwarranted clinical variation that may contribute to poor outcomes. This need is being addressed through EnRICH; a prospective clinical cohort of patients with lung cancer from metropolitan and regional NSW.

Aims:

- Investigate clinical variation in the treatment of patients with lung cancer
- Identify quality indicators with unwarranted clinical variation that would benefit from QI interventions

Methods: *Sample:* 750 consecutive newly diagnosed patients at six clinical sites across three Local Health Districts in metropolitan and regional areas of NSW.

Data collection: A suite of lung cancer specific, evidence-based quality indicators has been developed by an expert panel of lung cancer specialists, following review of national and international lung registries and clinical practice guidelines.

Clinical data are extracted from electronic and paper medical records longitudinally from diagnosis up to 2-year follow-up, describing patient and disease characteristics, and mapping patterns of care and outcomes against diagnostic, treatment and survival quality indicators.

Results: Among the 750 patients, 669 (89%) had NSCLC histology and 60 (8%) SCLC, the median age was 70 years and 54% were male. Three-quarters (78%) were current/ex-smokers and nearly one fifth (18%) lifelong never-smokers. 269 (36%) had stage I/II disease, 65 (8.7%) stage IIIA, 72 (9.6%) stage IIIB/C, and 328 (44%) stage IV. 505 (67%) resided in metropolitan areas. Analysis observed variations including, time from presentation to diagnosis and to commencing treatment, and proportion of patients reviewed at MDT meetings. Referral to supportive care services varied while referral to smoking cessation services was universally suboptimal.

Conclusions: Reasons for observed clinical variation are under investigation to determine whether warranted or unwarranted. The next steps are to implement and evaluate QI interventions in prioritised areas of need.

Paper ID 30

Distress screening in patients with Stage III melanoma: The ePROMs-MEL study

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Background: Previous research has reported levels of psychological distress requiring clinical referral or assistance in 30% of melanoma patients. For Stage III melanoma patients, distress may be more common. They must deal psychologically with the spread of their disease, often requiring extensive surgery, including sentinel node biopsy or lymph node dissection, which impacts significantly on their quality of life. Furthermore, they face difficult treatment decisions regarding immunotherapy which can have major survival benefits but is accompanied by the risk of serious and long-term adverse events.

Aim: To test the acceptability of routine collection of electronic Patient-Reported Outcomes Measures (ePROMs) data to identify patients with Stage III melanoma who are experiencing psychological distress and/or poor quality of life, to facilitate prompt referral to supportive care.

Methods: This mixed-methods project will recruit a minimum of 120 patients from Melanoma Institute of Australia and Royal Prince Alfred Hospital. Patients will complete PROMs using tablets in clinic waiting rooms at regular time-points over a 12 month period. Participants scoring ≥4 on the Distress Thermometer will be triaged to complete a further four questionnaires for more detailed assessment: the EuroQoL ED-5D-5L, EORTC Quality of Life Questionnaire – Cancer, Melanoma Concerns Questionnaire, and Depression, Anxiety and Stress Scale. Questionnaire responses will be automatically scored, enabling real-time patient-clinician discussion and appropriate referrals for supportive care.

Results: Assessment variables include referral rates for psychosocial distress and/or poor quality of life (pre- and post-intervention) and tracking of questionnaire responses over time. Feasibility and acceptability will be assessed through end-of-study surveys and interviews with all participating clinicians and 20% of patients.

Conclusions: The findings of this pilot study will directly influence the uptake of routine collection of PROMs in melanoma clinics at MIA and RPAH and will set a benchmark for adoption of electronic real-time distress screening in private healthcare settings.

Paper ID 31

Assessing chemotherapy-induced peripheral neuropathy - A psychometric analysis of current approaches

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Introduction: Worldwide cancer survivor numbers are steadily increasing, leading to a need for research to focus on survivor's quality of life, and reduction of treatment residual adverse events. Chemotherapy-induced peripheral neuropathy (CIPN) is a significant side-effect of numerous chemotherapies, often impacting 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 gold standard CIPN outcome measure.

Aim: This study aimed to evaluate the validity and responsiveness of different approaches to CIPN assessment and identify optimal outcome measures.

Methods : 859 cancer patients (54±13 years) treated with 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 as Spearman's correlation coefficient of >0.7 between measures and NCI grade. Discriminant validity compared measures using t-tests between NCI grade ≤1 and grade ≥2 CIPN. Responsiveness was evaluated in a subset of 356 patients who were prospectively assessed pre-treatment and mid-treatment scores with effect sizes (ES).

Results: PROMs demonstrated convergent validity ($r=0.74$-0.88, $P<0.01$), while sensory functional measures and clinical grading scales did not achieve acceptable correlations (all $r<0.7$, $P<0.01$). Discriminant validity was demonstrated in all measures (all $P<0.01$). Overall, PROMs were most responsive (ES=0.63-1.63) with sensory functional measures and clinical grading scales not demonstrating high responsiveness (ES=0.06-0.27), with the exception of 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. This present series suggests that the use of PROMs in combination with a responsive objective measure such as the TNSc provides optimal CIPN evaluation.

Paper ID 32

Determination of cancer stem cell characteristics in melanoma stem-like cells

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Background: It is well known that undifferentiated cancer cells, which exist in trace amounts in tumor tissue called cancer stem cells, could contribute to cancer recurrence, metastasis, and treatment resistance. On the other hand, conventional chemotherapy and radiation therapy cannot target cancer stem cells because the therapies target cells with cell cycle-active and differentiated cancer cells. Therefore, in recent years, attention has been focused on differentiation-inducing therapies that reduce the malignancy of cancer stem cells and increase their susceptibility against anticancer drugs. To evaluate phenotypes of cancer stem cells *in vitro*, tumor spheroids formed by three-dimensional culture systems are used. Tumor spheres from multiple cancer cell lines have high expression of cancer stem cells markers and drug resistance-related molecules. Of malignant tumors, we picked up melanoma, because the tumor has high metastatic potential, poor prognosis after metastasis and resistance to anticancer drugs. Thus, this study was aimed to investigate the cancer stem cells nature of spheroids formed by three-dimensional culture. We also conducted a study to reduce the malignancy of this spheroids.

Method: A human melanoma cell A375 derived from the skin was used in this study. Spheroids were formed by three-dimensional culture for two weeks, and experiments were conducted using these spheroids. As cancer stem cells markers, CD133, OCT4, and SOX2 were used, and mRNA levels of these marker were analyzed by the qRT-real time PCR method. The cell viability was evaluated by the MTT assay.

Results: The spheroids formed by three-dimensional culture showed high expression of cancer stem cells markers and chemoresistance-related molecules as compared with the adherent cells.

Discussion: It has been suggested that the spheroids formed by three-dimensional culture may be melanoma stem-like cells with cancer stem cell properties, because high expressions of cancer stem cells markers and drug resistance genes were observed.

Paper ID 35

Factors influencing older adults' cancer screening decision-making: A systematic review

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Background: Many older adults who are frail, have limited life expectancy or comorbidities, continue to be screened for cancer despite guidelines suggesting they should not. A greater understanding of the factors influencing older adults' cancer screening decision-making will provide helpful insight for clinicians navigating difficult discussions about screening, highlight future research needs and inform the design of interventions to optimise cancer screening in older adults.

Aim: To summarise the patient-reported factors influencing older adults' breast, prostate, colorectal and cervical cancer screening decisions.

Methods: Studies were identified by searching databases from January 2000 to June 2020 and independently assessed for inclusion by two authors. Data extraction and risk of bias assessment was independently conducted by two authors then all decisions crosschecked and discussed where necessary.

Results: The search yielded 2475 records, of which 21 studies were included. Nine studies were quantitative, eight qualitative, and four used mixed method designs. Most were conducted in the United States (17/21), and 10/21 assessed breast screening decisions only. Influential factors were synthesized into demographic, health/clinical, psychological, physician, and social/system categories. Commonly identified factors influencing the decision to undergo screening included personal/family history of cancer, positive screening attitudes, routine/habit, to gain knowledge, friends, and a doctor's recommendation. Factors influencing the decision to forgo screening included being older, negative screening attitudes, and desire not to know about cancer. Factors with varying influence included insurance cover, living in a nursing home, prior screening experience, health problems, limited life expectancy, perceived cancer risk, risks of screening, family, and a doctor's recommendation to stop.

Conclusions: Older adults' beliefs about cancer screening may run counter to concepts commonly incorporated in guidelines. Communication strategies are needed that support older adults to make informed cancer screening decisions by addressing screening beliefs in context with their perceived and actual risk of developing cancer.

Paper ID 37

Implementing telepresence robots to improve the well-being of adolescent cancer patients

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Background: When an adolescent faces cancer, their ability to attend school can be severely disrupted, resulting in disconnection from peers, missed educational milestones, reintegration difficulties post-treatment, and long-term societal impacts. The TRECA (Telepresence Robots to Engage CAncer patients in education) service was developed to support young patients impacted by cancer.

Aim: The aim of this study was to explore the perceived acceptability and feasibility of implementing telepresence robots with adolescent patients with cancer.

Methods: Phase I used semi-structured interviews (n=25) to assess the views of patients, parents, schools and clinicians of the benefits, barriers, and enablers of utilizing robots in schools for adolescent cancer patients. Results from phase I informed the development of the TRECA program. Phase II used semi-structured interviews (n=23) to assess the implementation experiences of young cancer patients, and their families, schools, and keyworkers who pilot-tested the TRECA program.

Results: In phase I, participants acknowledged a telepresence robot would provide critical connectivity with school friends and agency over their education during cancer treatment. Perceived implementation facilitators included accessible technology and adequate support, while barriers included, resistance of some stakeholders and difficulties resolving technical difficulties. In phase II the TRECA program was found to be an acceptable solution for enabling patients to attend school remotely. The TRECA program helped facilitate meaningful peer connections, providing a sense of agency and improving well-being. The necessity of stakeholder buy-in and taking an individualised approach to service delivery were also highlighted. Technological issues, stakeholder miscommunication and lack of knowledge were the key aspects of implementation needing improvement.

Conclusions: Using telepresence robots to connect adolescents to their schools during cancer treatment was regarded as highly acceptable, facilitating peer connection, and improving well-being. By making stakeholder-recommended improvements to existing processes and procedures, the TRECA program will continue to grow in effectiveness and capacity.

Paper ID 40

Reducing Tumor Oxygen Consumption to Enhance Radiotherapy in Diffuse Intrinsic Pontine Glioma

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Background: Diffuse Intrinsic Pontine Glioma (DIPG) is a rare, high grade glioma and fatal pediatric brain tumor that originates in the brainstem of children approximately 4-11 years of age with a survival of ~1 year from diagnosis. Since DIPG cannot be surgically removed due to its sensitive location, radiotherapy is the only treatment. However, most DIPGs recur within 12 months of treatment due to radio-resistance. Radiotherapy requires oxygen to be effective and hypoxia, which is common in the tumor microenvironment, is a major cause of radio-resistance. Hypoxia can be caused by both poor perfusion (supply) and high consumption by the tumor (demand). Previous studies have established that biguanides like metformin and phenformin decrease mitochondrial respiration in tumor cells, a major consumer of oxygen, and lead to an increase in oxygen levels. The increase in oxygenation increases radio-sensitivity and prolongs survival in animal models of DIPG and other tumors.

Aims: Our aim is to identify new and potent drugs that reduce tumor cell oxygen consumption so they can be combined to enhance the effects of radiotherapy.

Methods: Using the principle of drug repurposing, we screened a panel of 1963 FDA-approved drugs using the Seahorse assay. Seahorse measures tumor cell oxygen consumption (a marker of mitochondrial metabolism) and extracellular acidification (a marker of lactate and anaerobic metabolism), before and after drug treatment. This enables us to assess drugs that reduce oxidative metabolism, which may increase tumor oxygenation during radiotherapy.

Results and Conclusions: We have identified multiple compounds, already shown to be safe in humans, which reduce oxygen consumption in DIPG cells. We are testing identified drugs using in vitro and in vivo orthotopic pre-clinical DIPG models with the goal of moving into clinical trials. New treatment strategies to enhance the effects of radiotherapy may prolong survival in children with DIPG.

Paper ID 41

The role of urokinase plasminogen activator receptor, in HNcSCC Progression and metastasis

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Background: Cutaneous squamous cell carcinoma of the head and neck (HNcSCC) is the second most prevalent skin cancer and most common lethal malignancy worldwide. Currently, there are no reliable indicators to help identify primary cSCCs at high risk of developing metastases. Second-line therapies for unresectable advanced disease are also lacking.

Extracellular matrix (ECM) remodeling associated genes, including the urokinase plasminogen activation (uPA) system, are upregulated during tumor progression, but their role in cSCC invasion and metastasis is not known.

Aim: To investigate the role of ECM remodeling genes and UPAR in the cSCC progression and metastasis**.**

Methods: We conducted a targeted gene expression and functional analysis on RNA extracted from 35 cSCC patients with non-metastasizing and metastasising primary cSCC tumors and their coincident metastases and matched sun-exposed skin (SES). We confirmed our findings using UPAR immunohistochemistry (IHC) and miRNA assay.

Results: ECM receptor interaction and MMP remodeling were the most significantly upregulated pathways in metastatic tissues compared to non-metastasising tumors and SES. Genes involved in ECM remodeling including *PLAU, PLAUR, SERPINE1, and MMPs* were the highest differentially expressed genes in cSCC compared to SES, showing progressively increased expression with tumor progression. UPAR IHC analysis detected higher staining intensity at the invasive front of the more aggressive tumors (Metastases), Which confirms uPAR overexpression and its role in tumor progression. miRNA analysis revealed that hsa-miR-377-3p and hsa-miR-340-5p, known to inhibit *PLAUR* expression, were both significantly down-regulated in metastases versus primary cSCC and negatively correlated with uPAR IHC.

Conclusions: Our findings expand current evidence to support the role of PAS and MMPs as biomarkers of metastatic cSCC, and uPAR as a potential therapeutic target for translational purposes. Silencing UPAR with the hsa-miR-377-3p and hsa-miR-340-5p could be an option.

Paper ID 42

Non-coding and coding genomic mutational drivers of metastatic cutaneous squamous cell carcinoma

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Background: We have previously shown that non-coding variants dominate the genome of metastatic cutaneous SCC and highlighted the need for whole-genome sequencing (WGS) to fully elucidate the mutational landscape of this disease. Herein, we examined the patterns and frequency of non-coding variants in key regulatory regions, including the untranslated regions (UTR) and long non-coding RNA and describe their potential functional consequences.

Aim: To identify non-coding genomic mutational drivers and their functional impact in metastatic cSCC in the clinical context.

Methods: Matched tumour and blood WGS was used to detect somatic variants from regional metastases of 25 patients with head and neck cSCC. Variant calling was performed using MuTect2 and PURPLE pipelines to identify short variants, copy number and structural variation. The signals of driver mutations were detected for both coding and non-coding regions utilizing OncoDriveFML. Gene fusion analysis was carried out using the Arriba pipeline.

Results: We identified driver 3' UTR and long non-coding RNA mutations, which can significantly affect miRNA-mRNA interactions, RNA structure, and other downstream events. Our study detected new cSCC metastatic driver genes from somatic variants analysis, highlighting gaps in the extent of previously published WES/Targeted panel data. This advanced stage of cSCC has significant chromosomal amplification (8q, 5p and 14q) and deletion (4q, 8p and 18q). Novel combinations of mutations of the *TERT* promoter and aberrant micro RNA and long non-coding RNA were observed.

Conclusions: Metastatic cSCC is characterized by a highly mutated genome. The discovery of new potential coding and non-coding driver genes with an understanding of their functional impact in acquiring advanced cSCC expands our understanding of metastasis cSCC.

Potential Clinical Applications: We believe that these non-coding drivers could expand knowledge of non-coding regulation in cSCC disease and potentially be used for inhibition of oncogenes or activation of TSG.

Paper ID 43

A Sino-Australian comparison of diagnostic efficiency using digital breast tomosynthesis

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Background: There is good evidence showing heightened performance of radiologists in westernised countries when reading digital breast tomosynthesis (DBT) cases, however the diagnostic efficacy of this modality in China is understudied.

Aims: To improve the understanding of the diagnostic efficacy of DBT reading among Chinese radiologists and compare their performances with Australian radiologists.

Methods: This retrospective study used prospectively acquired data. A test set consisting of 35 DBT cases was used to assess reading performance. Twelve Chinese and twelve Australian radiologists read the test set independently. Case sensitivity, specificity, lesion sensitivity and ROC were used to assess performance and radiologists' characteristics were collected. Performance metrics and characteristics were compared using Mann-Whitney U tests and Fisher's Exact tests. Z-scores were used to investigate if the percentages of false negative per case and per cancer type differed significantly.

Results: Significantly lower specificity ($p=0.0003$), lesion sensitivity ($p=0.0172$) and ROC ($p=0.0001$) were recorded for Chinese radiologists compared to their Australian counterparts. Lower values for number of years reading DBT ($p=0.0194$) and cases read per week ($p=0.0122$) and numbers of hours of reading per week of mammography ($p=0.0094$) were shown among the Chinese group. Architectural distortion and stellate masses ($p<0.0001$ and $p=0.0188$, respectively) were significantly more difficult for the Chinese radiologists to detect compared to their Australian counterparts. Chinese readers significantly categorised more false-positives as discrete mass ($p<0.0001$) and less false-positives as architectural distortion ($p<0.0001$) in comparison with the Australian radiologists.

Conclusions: Chinese radiologists had lower performance when reading DBT compared to Australians radiologists. Architectural distortion and stellate masses were more challenging cancer types for Chinese readers.

Translational significance: The variation of reading performance and diagnostic errors identified in this study to some level highlight the need for effective education and training strategies in China in order to enhance breast cancer diagnostic efficiency.

Paper ID 46

Survival analysis of Glioblastoma Multiforme in elderly patients

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Background/Aim*:* Glioblastoma multiforme (GBM) is the most common brain tumour in adults worldwide, accounting for 60% of all primary brain tumours among adults and is often a rapidly fatal diagnosis. The incidence rate increases with age with an average age of 65 at diagnosis. This research presents a large single institution patient series examined for prognostic factors and impact of treatment in patients <70 and ≥70 years with GBM.

Methods: All participants (n=192) who underwent craniotomy for histologically diagnosed glioblastoma World Health Organisation (WHO) Grade IV between January 2011 – February 2020 at Illawarra Shoalhaven Local Health District Cancer Care Centre were included. The associations of key covariates (gender, disease extent, surgical resection, radiotherapy course and treatment with temozolomide, TMZ) with patient outcomes for those aged <70 or ≥70 years of age were estimated using the Kaplan-Meier method using the Log-Rank test for univariate and Cox regression method for multivariate analysis.

Results: Of the total 192 patients, 121 (63%) were <70 and 71 (37%) patients were ≥70 years of age, with a mean age of 64.4. Patients ≥70 years were less likely to receive adjuvant chemotherapy (47.5% vs. 79.6%, $p < 0.001$) and radiotherapy (64.8% vs. 81.0%, $p < 0.001$). This corresponded with a significant difference in overall survival (OS) between age groups (median OS 12 months vs. 5 months, $p < 0.001$). OS was significantly associated with disease extent, surgical resection, radiotherapy and TMZ ($p = 0.015$, 0.017, 0.024, 0.025, respectively) in those <70 years and only with radiotherapy ($p < 0.001$) and TMZ ($p = 0.013$) for those ≥70 years of age.

Conclusions: In this retrospective cohort, postoperative radiotherapy and TMZ were significantly associated with overall survival in those ≥70 years. These results support the current treatment protocols which involves consideration of maximal safe surgical resection followed by adjuvant radio-chemotherapy for all patients with GBM.

Paper ID 47

Preoperative Assessment of Peritoneal Carcinomatosis: A Comparative Analysis of Laparoscopy and CT

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Background: Peritoneal carcinomatosis index (PCI) remains as one of the most important prognostic indicators of patients with peritoneal surface malignancies. Preoperative assessment of PCI helps identify suitable surgical candidates for cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) to avoid unnecessary laparotomies, however, there has not been an agreement on whether laparoscopy or computed tomography (CT) offers a better assessment.

Aim: The goal of this research was to look into the region-specific performance of laparoscopy and CT in PCI determination and evaluate the efficacy of laparoscopy, CT, and their combination in preoperative peritoneal carcinomatosis assessment.

Methods: A literature search was done in MEDLINE, Embase and Scopus with the last search in May 2021. Articles comparing laparoscopy and CT in the preoperative assessment of peritoneal carcinomatosis in the same study were included. Accuracies, agreements with laparotomy PCI, and predictive values in completeness of cytoreduction of laparoscopy and CT were evaluated.

Results: In terms of PCI calculation, laparoscopy tended to perform better in region 7, 8 and 10, corresponding to the right lower, right flank and lower jejunum region; whereas CT tended to perform better in region 1, 2, 3 and 5, corresponding to the right upper, epigastrium, left upper and left lower region. Both laparoscopy and CT demonstrated similar overall accuracies in PCI categorization. A PCI score of 20 was shown to be the best cut-off for predicting the completeness of cytoreduction. Combination of laparoscopy and CT may offer marginal benefits in some situations, but its routine use has not been backed up by strong evidence.

Conclusions: Both laparoscopy and CT are reasonable preoperative modalities for the determination of PCI. However, their performances are region-dependent. Further researches are needed to evaluate whether the preoperative assessment of peritoneal carcinomatosis should be done by laparoscopy, CT, or a combination of both.

Paper ID 48

My Research Results Supporting researchers to return clinically actionable genetic research findings

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Background: Australian researchers increasingly support returning clinically actionable genetic research findings to participants, but may lack the skills and resources to do so.

Aim: Develop a program to support researchers and facilitate the return of clinically actionable research findings to participants.

Methods: The My Research Results (MyRR) program has been developed by a steering committee of clinicians, researchers, genetic educators and consumers. MyRR supports researchers to return clinically actionable research findings to participants. MyRR is staffed by genetic counsellors and available to researchers Australia-wide. Participants are notified of findings by letter, with a follow-up phone call from a genetic counsellor. The MyRR experience of returning findings from the Melbourne Collaborative Cohort Study and the ASPREE Study is reported.

Results: 23 individuals across the two studies were notified of clinically actionable findings from February-May 2021. Notification letters were sent to probands (n=21) or, if deceased, the nominated next-of-kin (n=2). MyRR genetic counsellors successfully contacted 21 individuals (12 women, 9 men) regarding pathogenic variants in BRCA1 (n=6), BRCA2 (n=13), MSH6 (n=1) and PMS2 (n=1). The average age of notified probands was 81 years. Findings were disclosed to 20 individuals, one declined to receive the findings. Thirteen probands expressed an intention to attend a clinical genetics service for confirmatory testing and risk management advice. Five individuals were already aware of the findings.

Conclusion: MyRR is a translational program promoting and facilitating access to clinically actionable genetic research findings, filling an important gap for Australian research studies and delivering health benefits to research participants.

Paper ID 49

Sodium butyrate exerts antitumor effect via the restoration of Dkk1 in colon cancer stem cells.

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Introduction: Colorectal cancer is the third common malignant tumor diagnosed globally and the fourth leading cause of cancer-related death worldwide. Currently, there is now accumulating evidence for the existence of colorectal cancer stem cells in human colorectal cancer, but they have not yet been identified. Recent studies have shown that abnormal epigenetic regulation is frequently occurred in tumor cells, including cancer stem cells. As a fermentation product of carbohydrate and dietary fibers by good intestinal bacteria, it is considered sodium butyrate, which is a short chain fatty acid and histone deacetylases (HDAC) inhibitor. Sodium Butyrate acts on the induction of Dkk1 (a Wnt antagonist) in colorectal cancer cells to exerts an antitumor effect. In this study, we tried to enrich cancer stem cells from colon cancer cell lines and establish a preventive method against colorectal cancer targeting cancer stem cells. In addition, we focused on the mechanism of the antitumor effect by sodium butyrate.

Methods: Colorectal cancer stem cells were enriched by a three-dimensional culture method using a human colorectal cancer cell line HT-29. Cell viability by MTT assay, mRNA expression by qRT-real time PCR, and cell differentiation by ALP activity were performed, respectively.

Results: Sodium butyrate treatment for 48 hours decreased the viability of colon cancer stem cells in a dose-dependency. At the same time, ALP activity, a differentiation marker, increased in a dose-dependency. The mRNA of HDAC2, an epigenetic-related gene, decreased in a dose-dependency at 24 and 48 hours. In addition, the mRNA expression of Dkk1 in low concentrations of sodium butyrate was increased twice at 48 hours compared to 24 hours.

Discussion: In butyrate-treated colon cancer stem cells, cell differentiation and cell death may occur simultaneously. In addition, it was also suggested that the balance between cell differentiation and cell cycle related to the restoration of Dkk1 function via the normalization of epigenetic regulation.

Paper ID 50

α-T3E induces cell death in mesothelioma through inhibition of proteasome and autophagy

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Background: Malignant mesothelioma, which is resistant to chemotherapy, is a non-curable cancer type, and its effective treatment approach has not yet been established. On the other hand, a vitamin E derivative α-T3E induces significant cell death in malignant mesothelioma cells (H28 and H2452). However, the cytotoxic mechanism of α-T3E for malignant mesothelioma cells remained unclear. Here, α-T3E affects proteasomes and autophagy-related molecules, and may induce significant cell death in malignant mesothelioma cells through simultaneous inhibition of proteasome and autophagy.

Aim: The aim of this study was to investigate whether α-T3E has inhibitory effect on proteasome and autophagy and clarify the cytotoxic mechanism of α-T3E for malignant mesothelioma cells

Method: Malignant mesothelioma cells H28 and H2452 cells were treated with α-T3E (20 μM), and the viability of these cell lines was measured by the WST-8 method. In addition, phosphorylation status of STAT3 and nuclear accumulation of Nrf1, both of which are transcription factors to activate proteasome, accumulation of LC3II and localization of Rab proteins, both of which are proteins to stimulate autophagy, were evaluated by Western blotting. Furthermore, the expression level of the proteasome active site was evaluated by RT-PCR and chymotrypsin-like activity was measured.

Results: α-T3E induced significant cell death in H28 and H2452 cells. α-T3E suppressed the phosphorylation of STAT3 and the nuclear accumulation of Nrf1. In addition, α-T3E reduced the expression level of the proteasome active site and chymotrypsin-like activity. Furthermore, α-T3E suppressed the cell membrane localization of the Rab proteins and promoted the accumulation of LC3 Ⅱ

Conclusion: α-T3E induces significant cell death in malignant mesothelioma cells through simultaneous inhibition of proteasome and autophagy. So, combination of proteasome and autophagy inhibition is effective treatment strategy against malignant mesothelioma.

Paper ID 51

Antibody Drug Conjugates: Fine tuning the targeted missiles

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Background: The interest in the development of Antibody Drug Conjugates (ADCs) has embellished research over the last 20 years. There are currently a variety of conjugation approaches to improve treatment specificity and enhance payload delivery as a result of the success of ADCs. However, there are various limitations including mechanisms of resistance, poor tumour penetration and a narrow therapeutic index that pose as a barrier to the success of these therapeutics. So how do we address this? Emerging approaches focus on ways to overcome some these challenges as well as conjugation techniques which aim to attain ADC homogeneity to control the number of payloads attached and the site of attachment to addresses issues encircling therapeutic index and ADC clearance. Keywords: ADC, limitations, resistance, emerging conjugation techniques, ADC homogeneity, therapeutic index

Paper ID 52

Improving Delivery of Amiloride Analogues as uPA Selective Inhibitors for Use in Metastatic Disease

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Introduction: Metastasis accounts for 90% of all cancer-related deaths. The metastatic process in multiple cancer types is facilitated by urokinase plasminogen activator (uPA), a cell-surface mediator of extracellular matrix degradation and tumour cell invasiveness. We previously developed novel, non-cytotoxic 5- and 6-substituted amiloride analogues that potently inhibit human uPA activity and were effective in cancer metastasis models. These compounds show potential for use as anti-metastasis therapy, however, improved drug delivery systems are required for future clinical use.

Aim: To determine the effect of encapsulated reformulation of the analogues relative to standard aqueous formulations on enzymatic activity using *in vitro* methods.

Methods: Compounds were tested for inhibition of human uPA in fluorogenic purified enzyme assays and inhibitory activities confirmed in whole-cell assays using a breast cancer cell line with high uPA expression. Potent compounds were reformulated with 30% w/v Kolliphor HS-15 to produce a novel drug-loaded micellar system.

Results: Preliminary data shows reformulation of compounds, at matched molar concentrations, in 30% w/v Kolliphor HS-15 vehicle did not impede on-target uPA inhibitory activity relative to standard formulation. This encapsulated emulsion system showed similar results for analogues with varying physicochemical properties across multiple orders of magnitude ($logD_{7.4}$ range = 2.8 - 5.1). Substituted pyrimidine analogues showed stronger uPA selectivity in both formulations, within a 2-fold range (uPA IC_{50} <300 nM).

Conclusion: Our compounds showed strong uPA inhibitory activity at the nanomolar level that was maintained in an encapsulated formulation. Further, the formulation remained effective despite varied drug physicochemical profiles, including high lipophilicity which otherwise limits drug action and *in vivo* use. These results support further evaluation of these compounds as novel targeted therapeutics for non-cytotoxic and anti-metastatic therapy of uPA-driven cancers. Future work will involve further formulation optimisation for *in vivo* use, including application of nanoparticle encapsulation, to improve drug delivery and dosage.

Paper ID 53

Developing Off the Shelf CAR T-cells: Nonviral and Site-specific Knockout of TCR and Knock-in of CAR

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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 >$500,000 AUD 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 utilising two single guide RNA and short (35bp) homology arm length is sufficient to achieve up to 85% 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.

Conclusion/Translational Significance: Our data demonstrates that alternative precise, cutting-edge technologies can be used to generate novel and safe 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 infections and malignancies.

Paper ID 55

Recombinant Biomarker DDA Library Increases DIA Coverage of Cancer-Associated Plasma Proteins

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Credible detection and quantification of low abundance proteins from human blood plasma is a major challenge in precision medicine biomarker discovery when using mass spectrometry (MS). In this study, we employed a mixture of selected recombinant proteins in DDA libraries to subsequently identify cancer-associated low abundance plasma proteins using SWATH/DIA. The exemplar DDA recombinant protein spectral library (rPSL) was derived from tryptic digestion of 36 recombinant human proteins that had been previously implicated as possible cancer biomarkers from both our own and other studies. The rPSL was then used to identify proteins from non-depleted colorectal cancer (CRC) EDTA plasmas by SWATH-MS. Most (32/36) of the proteins used in the rPSL were reliably identified from CRC plasma samples, including 8 proteins (i.e., BTC, CXCL10, IL1B, IL6, ITGB6, TGFα, TNF, TP53) not previously detected using high-stringency protein inference MS according to PeptideAtlas. The rPSL SWATH-MS protocol was compared to DDA-MS using MARS-depleted and post-digestion peptide fractionated plasmas (here referred to as a human plasma DDA library). Of the 32 proteins identified using rPSL SWATH, only 12 could be identified using DDA-MS. The 20 additional proteins exclusively identified using the rPSL SWATH approach were almost exclusively lower abundance (i.e., <10ng/ml) proteins. To mitigate justified FDR concerns, and to replicate a more typical library creation approach, the DDA rPSL library was merged with a human plasma DDA library and SWATH identification repeated using such a merged library. The majority (33/36) of the low abundance plasma proteins added from the rPSL were still able to be identified using such a merged library when high-stringency HPP Guidelines v3.0 protein inference criteria were applied to our dataset.

Paper ID 56

Partial Remission in Thymic-NET with Alpha-PRRT (Ac-225) refractory to Beta-PRRT (Y-90/Lu-177)

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Background: Thymic-NET is an extremely rare tumour accounting for up to 0.02 to 0.18/100,000/year in the Europe or USA, respectively, and treatment of recurrent Thymic-NET remains challenging.

Aim: Based on the principle of personalised precision medicine, this case reports partial remission of a recurrent Thymic-NET following alpha-PRRT using Actinium-225, refractory to standard-of-care therapy including beta-PRRT with Yttrium-90 and Lutetium-177.

Methods: 46 y.o. female diagnosed with Thymic-NET in 04/2002 underwent palliative resection of primary tumor (R2) and adjuvant EBRT, SSA-Therapy with Sandostatin-LAR® (03/2003-11/2005) and Interferon (08/2004-02/2006). Restaging with Ga-68-SSTR-PET/CT in 03/2006 demonstrated disease progression. Following recommendation of Neuroendocrine Tumorboard, the patient received eight courses of personalised beta-PRRT using Y-90 (1x) and Lu-177 (7x) from 03/2006 till 09/2019, resulting in PFS intervals of 30, 21, 24, 18 and 24 months following the 1st, 2nd, 3rd, 4th and 5th phases of PRRT, respectively. Between the 1st and 2nd phase of PRRT, molecular complete remission of disease was observed on Ga-68-SSTR-PET/CT in 2008.

In 09/2019, the patient's clinical condition deteriorated; restaging with Ga-68-DOTATOC-PET/CT demonstrated significant progression of disease with extensive, SSTR-positive pleuropericardial and mediastinal lymph node metastases, and left-sided pleural effusion.

Applying principle of personalised precision medicine, the Neuroendocrine Tumorboard recommended further PRRT using alpha-emitting Actinium-225. The 9th PRRT with 19 MBq of Ac-225 DOTATOC was performed in 10/2019.

Results: Following Ac-225 DOTATOC PRRT, the patient was fatigued with reduced appetite up to 4 weeks, which resolved spontaneously with subsequent stabilisation of clinical condition. Restaging with Ga-68-DOTATOC-PET/CECT at 12 months post alpha-PRRT demonstrated partial remission of disease with remarkable reduction of tumor burden and regression of pleural effusion. Further restaging with Ga-68-DOTATOC-PET/CECT at 18 months post-therapy in 04/2021 demonstrated persistent stable disease. Furthermore, there was no evidence of any clinically significant hematotoxicity or nephrotoxicity at any point-in-time following alpha-PRRT with Ac-225 DOTATOC.

Conclusion: Hence, applying the principle of personalised precision medicine, palliative alpha-PRRT with Ac-225 can be considered feasible, effective, and safe in patients with Thymic-NET refractory to beta-PRRT with Lu-177 and/or Y-90.

Paper ID 57

High-throughput single-cell lipidomics of prostate cancer cells

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Background: As single-cell transcriptomics technologies have evolved we have begun to appreciate the wide degree of heterogeneity present within seemingly identical cells (i.e., those from the same clonal population/genetic background). This insight has provided us with a new understanding of the fundamental biological processes of growth, development, and ageing, as well as new information on cancer initiation and metastasis. Despite these advances, however, our ability to fully probe this cellular diversity is limited with the development of methods to assay metabolites from single cells (i.e., single-cell metabolomics) being hindered by technological challenges. Development of methods that can assay metabolites from single cells would deliver a greater understanding of cancer biology and metastasis initiation and could be useful as a diagnostic or prognostic tool when applied to circulating tumour cells.

Aim: To develop a high-throughput method for analysis of lipids in single cells and apply it to the study of prostate cancer cells.

Methods: we have combined fluorescence-activated cell sorting with chip-based nanoelectrospray ionisation mass spectrometry to deliver a high throughput method capable of detecting membrane lipids from single cells.

Results: Using a shotgun lipidomics strategy we can detect up to 60 phosphatidylcholine (PC) and sphingomyelin (SM) membrane lipid species from singly isolated cells. Overnight culturing of HepG2 and C2C12 cells in the presence of docosahexaenoic acid (DHA, 22:6n-3) results in distinct changes in lipid profile that are easily discernible in singly isolated cells. We also show the utility of applying this method to single sorted prostate cancer cell lines (PC3, LNCaP, DU145, and non-tumorigenic PNT1) to identify unique lipidomic signatures. Future work will focus on expanding the coverage of membrane lipid classes and polar metabolites able to be detected using this workflow through the use of charge-switching derivatisation strategies to improve metabolite signal.

Paper ID 59

The mucosal microbiome in bowel polyp patients

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Background: Bowel polyps are areas of benign abnormal growth in the colorectum that can develop into cancers. Current guidelines for colonoscopic 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 reported the presence of various gut microbes with bowel cancers, suggesting a potential role in their development. However, less is known about the composition of the gut microbiota during the premalignant polyp phase, especially the mucosa, as most microbiome studies utilise faecal sampling.

Aim: This study aims to characterise differences in the gut mucosa microbiome between patients with and without bowel polyps to identify bacterial biomarkers that may associate with polyp development and progression.

Methods: Mucosal biopsies were collected from participants undergoing colonoscopy, 20mm 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 gut mucosa from 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. Lachnospira, Coprococcus comes, Christensenellaceae and Eubacterium were typically depleted in polyp patients compared to healthy controls.

Conclusions: These findings demonstrate subtle differences in mucosal bacterial abundance between patients with and without bowel polyps, and highlights the potential to define biomarkers for disease risk.

Paper ID 60

Using BET inhibitors to potentiate CART-cell therapy for neuroblastoma

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Background: Neuroblastoma (NB) is the most common paediatric extracranial solid cancer and has low survival rates, particularly in high-risk NB that is often resistant to standard treatments. This prompts an urgent need for new approaches such as chimeric antigen receptor (CAR)T-cell therapy, in which patient T cells are genetically engineered to specifically destroy cancer cells. CART-cell therapy is clinically used to treat some leukaemia and lymphomas, but so far has limited efficacy against solid tumours due to immune suppression by tumour cells.

Aim. Using in vitro co-culture models and in vivo xenograft models of NB we have shown that CART-cells targeting GD2 rapidly up-regulate immune checkpoint receptor Programmed Cell Death 1(PD-1) following exposure to tumour cells. Additionally, we found that NB cells surviving CART-cell therapy acquire adaptive immune resistance by up-regulation of Programmed Cell Death Ligand 1 (PDL1) in response to pro-inflammatory cytokines released by cytolytic CART-cells. Since PDL1 acts to activate PD-1 checkpoint in CART-cells, we proposed that blocking this checkpoint will enable enhanced antitumor killing mediated by CART-cells.

Methods and Results: To test this hypothesis, we have used small molecule inhibitor of bromodomain and extra-terminal motif-containing proteins (BETi) JQ1 that acts to down-regulate PDL1 in NB. Here we show that priming NB cells with JQ1 enhances CART-cell effector function and promotes target cell killing in co-culture model and xenograft mouse model of NB. JQ1 given 1 day prior to CART-cell infusion delayed NB growth and promoted CART-cell infiltration of tumours.

Conclusion. Using BETi to down-regulate PDL1 activating PD-1 checkpoint in CART-cells in NB cells may be a novel therapeutic option to potentiate CART-cell therapy against NB.

Paper ID 61

Tumour specific phosphorylation of alpha-enolase (ENO1) regulates nuclear export in breast cancer

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Alpha-enolase (ENO1) is a glycolytic enzyme identified as a potential biomarker in several cancers where it is thought to perform moonlighting functions unrelated to its role in glycolysis. ENO1 is thought to be highly cytoplasmic in cancer, however the underlying mechanism of action and regulation of its subcellular distribution within tumour cells remains poorly understood. This study examines the role of tumour-specific post-translational modifications in the regulation of ENO1 nuclear export and consequential cytoplasmic localisation in breast cancer.

ENO1 mRNA and protein were both highly expressed in tumorigenic cells of the MCF10 triple negative breast cancer (TNBC) isogenic tumour progression model. Immunofluorescence experiments demonstrated ENO1 was evenly distributed throughout the cytoplasm and nucleus in MCF10A non-tumour cells, while in contrast it was distinctly cytoplasmic in a majority of TNBC tumour cell lines, suggesting a tumour-specific regulatory mechanism. Using TCGA phosphoproteomics data we determined that ENO1 is phosphorylated at serine 419 in TNBC tumours. Confocal laser scanning microscopy experiments using GFP-tagged ENO1 mutants found that the non-phosphorylatable ENO1-S419A mutant exhibited nuclear accumulation in tumour cells to an extent similar to WT-ENO1 in non-tumour cells. In contrast, the phosphomimetic ENO1-S419D mutant was highly cytoplasmic only in tumour cells similar to WT-ENO1. We show that ENO1-S419A exhibits reduced nuclear export in tumour cells to the same extent as treatment with a specific inhibitor of nuclear export (Leptomycin B).

Together our results suggest that phosphorylation of ENO1-S419 specifically in tumour cells is required for efficient nuclear export. Clinical translation of this finding requires elucidation of the functional outcome of this post-translational modification. Nevertheless, this research opens possibilities for the development of ENO1 tumour-specific phosphorylation targeted therapeutics in a range of cancers including TNBC.

Paper ID 62

The role of altered lipid metabolism in chemoresistant pancreatic ductal adenocarcinoma

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Background: Pancreatic ductal adenocarcinoma (PDAC) is deadly disease for which there is no cure and few therapeutic options. Gemcitabine, one of the major frontline therapies used in the clinic for treatment of pancreatic cancer, is a compound that PDAC cells rapidly become resistant to which greatly limits the efficacy of therapeutic treatment for PDAC patients. New investigations into the metabolic dependencies and vulnerabilities in PDAC cells is slowly revealing how and why this chemoresistance arises. One area that has been of growing interest is lipid metabolism, for which unique alterations in it appear to mediate cancer cell survival, growth and importantly, chemoresistance.

Aim: To investigate alterations in lipid metabolism in two gemcitabine-resistant (GEMR) PDAC cell lines.

Methods: We established two GEMR PDAC cell lines by continuous culture of MiaPaCa2 & Panc1 in increasing amounts of gemcitabine over a period of several months until a statistically significant increase in the half-maximal inhibitory concentration (IC_{50}) was observed. Western blotting, radiolabelled palmitate tracing, and untargeted lipidomics were then used to better understand the impact of GEMR on lipid metabolism.

Results and Conclusions: Investigation of key metabolic pathways (i.e. glucose, glutamine, and fatty acid metabolism) in these cells revealed an alteration in lipid metabolism in GEMR MiaPaCa2 cells. Specifically, downregulation of fatty acid synthase (FAS) was observed within GEMR cells alongside a concomitant increase in inactivation of acetyl-CoA carboxylase. Ongoing work is focused on more fully investigating lipid metabolism including changes in fatty acid uptake and oxidation. We are also assessing the effect of GEMR on membrane lipid profile in both MiaPaCa2 and Panc1 cells. Together this will help to identify new therapeutic targets that can improve pancreatic cancer treatment efficacy.

Paper ID 65

Patient health literacy correlates with times to diagnosis of head and neck cancer

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Background: Health literacy (HL) refers to the skills and knowledge required to understand, access, and make decisions about healthcare. HL may impact timeliness of cancer diagnosis and treatment, but there is a dearth of research regarding this.

Aim: To explore correlations between domains of patient HL and time intervals along the pathway to treatment for patients with head and neck cancer (HNC).

Methods: Patients within six months of HNC diagnosis who underwent treatment at one of four sites in NSW were invited to participate. Patients completed two questionnaires: 1) an assessment of their pathway to treatment of HNC (adapted from an instrument developed by the International Cancer Benchmarking Partnership) and 2) the Health Literacy Questionnaire® (HLQ®), a 44-item validated tool to assess HL across nine domains. Data on dates and events were cross-checked with medical records, and dates allocated according to an established hierarchy. Non-parametric correlations were assessed using Spearman's rank-order correlation coefficient.

Results: From October 2018-March 2020, 95 patients (63% male, mean age 65 years) completed both questionnaires. The patient interval (symptom recognition to first healthcare practitioner (HCP) visit) was significantly negatively correlated with two HLQ® domains. The primary care interval (first HCP visit to specialist referral) was significantly negatively correlated with two HLQ® domains. The diagnostic interval (first HCP visit to diagnosis) was significantly negatively correlated with five HLQ® domains. The treatment interval (diagnosis to treatment) was not correlated with any HLQ® domain. Domains 2 (sufficient information to manage health) and 8 (ability to find good health information) were most strongly correlated with the above time intervals.

Conclusion: Higher levels of HL, especially the ability to find and use health information, correlates with shorter times to HNC diagnosis. Health systems/policy should provide additional support for patients with low HL to reduce disparities in timeliness of various intervals.

Paper ID 68

HFE gene expressions and polymorphisms in gastric cancers; a pilot study

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Background: GC has a poor prognosis and causes a significant global health burden, being the fourth cause of cancer mortality worldwide. The *HFE* gene polymorphisms H63D and C282Y have been linked to various cancers, but its pathogenic role in gastric cancers (GC) is not studied in detail. Therefore, further experimentation on *HFE* gene variants and GC is necessary to confirm the hypothesis that iron overload induces tumorigenesis.

Aims: The overall aim of this study is to identify if GC risk is associated with *HFE* gene expressions and polymorphisms with relation to cytotoxic iron overload.

Methods: A retrospective case-control study was conducted on 20 patient samples with GC tissues and matched normal gastric tissues, collected from patients who underwent diagnostic stomach endoscopies or gastrostomies at Kaohsiung Medical University, Taiwan. For gene expression analysis, a quantitative polymerase chain reaction (qPCR) was performed to investigate *HFE* gene expression levels in the 20 GC tissues and matched normal gastric tissues. The H63D and C282Y polymorphisms were detected through Sanger sequencing.

Results : An upregulation of *HFE* mRNA expression levels was noted in ~ 35% (7/20) of GC patients, whereas ~ 65% (13/20) showed low *HFE* expression. Furthermore, through current Sanger sequencing analysis, neither any C282Y polymorphisms nor any H63D polymorphisms have been identified. Nonetheless, one sample has a *HFE* variant known as rs369354634 (c.843G>A), and another variant (c.184G>A) has also been found in five samples.

Conclusion: This pilot study has confirmed varied expression profiling for *HFE* gene expressions in GCs, and it may potential association with gene polymorphisms. However, larger sample size and additional data are required to support the hypothesis and confirm significance.

Paper ID 70

Tracking circulating tumour DNA in patients with resectable gastroesophageal cancer

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Background: Gastroesophageal adenocarcinomas (GOCs) are amongst the most common and lethal tumours worldwide. Current clinically useful, but suboptimal, biomarkers are tissue HER2 and biochemical CEA and CA19.9.

Interest in liquid biopsies is increasing, offering minimally invasive, real time analysis of cancers. Circulating tumour DNA (ctDNA) are copies of the tumour genome released into the peripheral blood. In other solid tumours (e.g. lung), ctDNA can identify tumour mutations and assist in guiding treatment options as this ctDNA represents the current heterogeneous tumour genomes. Serial tumour mutation monitoring is predictive of cancer recurrence, allowing for detection at earlier time points than possible by traditional monitoring and, with limited treatment options on relapse, possible patient stratification for promising clinical trials.

Aim: Explore association of key cancer driver ctDNA mutations throughout curative treatment and follow up.

Methods: Pre-operative plasma samples from 10 patients with GOCs were assessed using Thermo Fisher Oncomine Pan-Cancer Cell Free next generation sequencing (NGS, 52 gene panel) to identify common, actionable mutational pathways. Targetable mutations were subsequently assessed in follow up samples using droplet digital polymerase chain reaction (ddPCR) to track their changes. We report three interesting case studies.

Results: *MET* mutations were identified in two patients (66 years old each), both of whom are long term survivors. *MET pT1010I* was identified in a patient with oesophageal adenocarcinoma, and *MET p.R988C* in a patient with gastric adenocarcinoma. At presentation, the latter patient had concurrent mutations in *RAS (p.G13S)* and *TP53 (p.y220C)* that reduced following pre-operative chemoradiation, surgery and adjuvant chemotherapy. A further patient had a detectable *TP53 (p.R282W)* mutation whose molecular frequency increased prior to clinical relapse.

Conclusions: Important actionable tumour genomic mutations can be identified by NGS and tracked using ddPCR. This strategy may help in guiding best treatment options, including choice of possible clinical trials, for GOC patients.

Paper ID 72

Targeting the PI3K/AKT/mTOR pathway in cutaneous squamous cell carcinoma

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Background: Cutaneous squamous cell carcinoma (cSCC) is a skin cancer that can metastasise in up to 5% of cases. Treatments are primarily surgery and/or radiotherapy as chemotherapeutics have largely been unexplored. While immunotherapy has shown remarkable efficacy against advanced cSCC, many sufferers are immunocompromised and ineligible for this therapy. Thus, there exists the demand for other contemporary interventions. The significance of the PI3K/AKT/mTOR pathway in cSCC has been increasingly reported upon and may confer radio-resistance. Therapy directed against this pathway is therefore worthy of investigation.

Aim: To investigate the physiological influence of PI3K/AKT/mTOR inhibitors against metastatic cSCC cell cultures.

Method: PI3K/AKT/mTOR inhibitors were screened against patient-derived metastatic cSCC cultures with efficacy determined via cell viability assays. The phosphorylation status of PI3K/AKT/mTOR components was determined by western blot analyses +/- an inhibitor. The utility of PI3K/AKT/mTOR inhibitors as radio-sensitisers was briefly investigated using the clonogenic survival assay. Physiological responses were compared with molecular data obtained from whole genome sequencing, RNA-seq, NanoString gene expression, and methylation sequencing.

Results: Numerous drugs were found to potently inhibit cell viability, particularly those acting upon the catalytic subunit of PI3K, chiefly the drug PIK-75. This drug was found to greatly alter the phosphorylation status of pathway components in as little as 10 minutes, triggering a halt in cell cycle progression and inducing apoptosis. These responses correlate with genetic alterations in the PI3K/AKT/mTOR pathway, including: copy number alterations in *AKT1*, *PIK3CA*, and *PIK3CG*, along with numerous single-nucleotide variants – aligning with mutations observed in wider clinical cohorts. PIK-75 in association with low-dose radiation produced a radiobiological response warranting further investigation.

Conclusion: PI3K/AKT/mTOR components are dysregulated in metastatic cSCC and are a candidate therapeutic target. Response to inhibitors of this pathway appear related to mutational status, although investigation of bypass mechanisms is necessary.

Paper ID 73

Implementation of microdosimetry in proton therapy clinical practice

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In Australia, more than 100 children aged 0-14 are diagnosed with malignant brain tumours each year. Brain cancer survival rates in children are good, with 75% surviving 5 years compared to 20% of adults. Survival rates have improved significantly in the last 30 years, making the avoidance of long-term complications even more important.

Proton therapy decreases radiation exposure to normal parts of the brain compared to conventional X-ray therapy, thereby improving long-term cognitive outcomes. The radiobiological efficiency (RBE) of protons depends on their linear energy transfer (LET) which varies throughout the treatment volume. Conventional proton therapy planning assumes a constant RBE of 1.1, while biologically optimized robust planning is a paradigm shift taking into account variable RBE and LET. However, its clinical implementation requires a new quality assurance capability called dose averaged LET_D verification.

The Centre for Medical Radiation Physics (CMRP), University of Wollongong, developed an award winning microdosimeter called MicroPlus for verification of LET_D in proton and heavy ion therapy. MicroPlus is the only such device in the world and is patented, licensed, and currently used in eleven of the world's leading proton therapy centres.

At the University Medical Center Groningen, MicroPlus was tested in an anthropomorphic head phantom to verify the LET_D calculated by the RaySearch treatment planning system for brain, nasal and head and neck tumours. We demonstrated that if the RBE actually increases up to 1.5, this would lead to 40% overdosing at interfaces between the tumor and normal tissue.

MicroPlus and the experience gained at CMRP during two decades of particle therapy research, allows Australia to provide the best proton therapy treatment for brain tumours at the Bragg Centre for Proton Therapy being built in Adelaide and the planned National Particle Treatment and Research Centre at Westmead.

Paper ID 74

Inhibition of focal adhesion kinase in cutaneous squamous cell carcinoma

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Background: Cutaneous squamous cell carcinoma (cSCC) is a common non-melanoma skin cancer. Metastases occur in 2-5% of these patients and often require a combination of radical surgery and radiation therapy. There are few effective therapies for refractory cSCC due in part to a lack of research integrating key molecular mechanisms with therapeutic response. Recent efforts by our group have revealed that dysregulated signalling via focal adhesion kinase (FAK) and affiliated phosphoinositide 3-kinases (PI3K) contributes towards cSCC tumorigenesis and metastasis. Inhibitors of FAK signalling, including Y15, are therefore a potential therapeutic to be explored.

Aim: To characterize the effects conveyed by FAK inhibitor Y15 on patient-derived metastatic cSCC cell lines.

Methods: Effects on the actin cytoskeleton, cell motility, and intracellular signalling circuits were assessed using fluorescence microscopy, scratch wound assays, and western blots, respectively. A timeline of the anoikis was characterized using life cell imaging in association with apoptosis and life-dead stains.

Results: The FAK inhibitor Y15 demonstrated a low micromolar potency against the cell lines accompanied with a reduction in cell adhesion, motility, and morphology in a time- and dose-dependent manner. High-dose Y15 quickly induced cell detachment leading to cell death. Sub-lethal doses of Y15 were associated with the formation of stress fibres and a reduction of cell motility consecutive to Y15 treatment was observed. Both observations point towards a potential involvement of two GTPases, Rac and RhoA, regulating cell motility and stress fibre formation, respectively. Rac involvement and a reduction of phospho-Akt/Akt ratios point towards an involvement of the PI3K/mTOR pathway and advise combination of Y15 with inhibitors of the same.

Conclusion: Y15 proves effective in targeting anoikis resistance in metastatic cSCC cell lines in 2D cell cultures. A combination of Y15 with PI3K/mTOR inhibitors warrants further investigation as well as assessing Y15 in more clinically relevant assays.

Paper ID 77

Potential anti-cancer and immunomodulatory effects of TMS magnetic fields

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Background. Transcranial magnetic stimulation (TMS) is a non-invasive pain-free medical technology clinically approved for the treatment of drug-resistant depression. Conventional TMS uses non-heating strong (≤4 T) pulsed (≤300 Hz) magnetic fields (MF) to induce electric currents in the cortical neurons and control their activity. However, the effects of the TMS-like MF on non-neuronal cells and artificial systems are almost unknown. We hypothesized, that repetitive magnetic stimulation (RMS) by TMS devices can have anti-cancer and immunomodulatory effects. These effects rely on alternative biophysical (magnetically-induced) mechanisms and may help to overcome the problem of cancer drug- and radioresistance.

Aim. This study explores the potential and feasibility of RMS as an adjuvant/allied treatment in oncology.

Methods. We examined effects of 22 RMS regimes designed *de novo* on viability and phenotype of tumour and immune cells, including glioblastoma (GBM), pancreatic ductal adenocarcinoma (PDAC), hepatocellular carcinoma (HCC) and colorectal cancer (CRC) cells, microglia (BV2 cell line) and human primary peripheral macrophages. We also tested the effect of PRMS on a drug release from polymer nanoparticles in aqueous environment. A standard TMS device "Magstim Rapid^2" with AFC70 coil was applied to the cell cultures spatially configured to correspond to a peak MF of 0.6-0.8 T, 0.25-50 Hz frequency, with sessions of 300 or 600 pulses.

Results. RMS selectively modulated the viability and functional polarisation of immune-stimulated microglia and macrophages in a frequency/intensity-dependent manner and affected the proliferation/viability of cancer cells (cancer type, frequency- and pulse number-dependent up- and downregulation). The triggering of the drug release from polymer nanoparticles by the 50 Hz/2 min RMS mode was observed.

Conclusions. Our pioneering findings demonstrate the potential of RMS performed with using of re-purposed TMS equipment for immunomodulation, cancer treatment, and treatment aided with nanomedicines.

We thank Sydney Vital (for seed grant) and Medilink Australia (for providing the "Magstim").

Paper ID 79

Optimising community service use with ePRO-based screening during routine Radiation Oncology care

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Background: Community support services play an important role in the holistic care of cancer patients. Low referral rates from cancer services to the smoking cessation program Quitline and the Canteen support service for families affected by cancer suggest potential for optimisation.

Aim: To sustainably embed systematic screening and linking with Quitline and Canteen into the routine care process of the Radiation Oncology department at Royal North Shore Hospital.

Methods: We added two screening questions to our existing electronic patient-reported outcomes (ePRO) survey that is routinely sent to all eligible new patients. If a patient met Quitline or Canteen screening criteria, a Patient Care Radiation Therapist (PCRT) provided information and offered referral. We partnered with the Canteen and Quitline teams to familiarise PCRTs with their services and co-designed a tailored information and referral approach. The program was evaluated via referral numbers and questionnaire to all clinical staff (34 of 77 staff responded).

Results: Between August 2020 and January 2021, the screening survey was completed by 366 patients (88% response rate). We found 24 patients (6.6%) were current smokers of which 9 patients accepted referral to Quitline. This was an over 100% increase of the health district-wide rates for the same period in 2018. 85 patients (23%) had children aged 0-25 years, and 18 patients accepted referral to Canteen. This was an annualised increase of 350% from 2018. 97% of staff reported that it provides emotional and/or professional comfort knowing that eligible families have been offered support by Canteen. 100% of staff rated the overall impact of the referral program for their patients as beneficial.

Conclusions: Systematic ePRO-based screening and a co-design strategy enabled successful translation of this referral process into routine care. Substantially increased referral rates to Quitline and Canteen provide benefits to both patients and clinical staff.

Paper ID 80

Challenges in 3D cell culture: validation of cell viability assays in 3D brain tumour model

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Background: Preclinical assays have largely failed to effectively predict the efficacy of anticancer drugs. This could be caused by lack of tumour-extracellular matrix components in 2D cell culture. Moving to 3D models, one of the challenges is how to assess drug efficacy. Cell viability is an essential parameter to measure cell growth and to assess the drug effectiveness. Viability assays are typically used in low cell density 2D cultures and may not produce the same results in 3D cultures with high cell density and added matrix components.

Aim: Our aim is to validate the common viability assays in three different models: conventional 2D culture, matrigel-based 3D culture and an organ-specific 3D brain tumour model recently developed by us.

Methods: Cell populations of human glioma U251 cells were plated in 2D in various cell numbers. Identical cell numbers were mixed with matrigel to form a 3D culture model. Organ-specific 3D scaffolds were developed by decellularizing animal brain tissue followed by seeding with U251 cells. Scaffolds were cultured for up to 3 weeks. We tested the performance of four different viability assays (MTT, Alamar Blue, ATP, LDH) on three different culture models and calibrated the assay output versus known cell numbers by counting and DNA quantification.

Results: In all of our selected cell viability assays, the assay output was higher in 2D samples compared with matrigel samples containing the same number of cells. In MTT assay by increasing the reagent concentration the difference between assay reading in 2D and matrigel samples became less which might indicate that there is a decreased reagent availability to the cells grown in Matrigel.

Conclusions: Most protocols for viability assays that are validated for 2D cell culture are not (directly) applicable to 3D models, however, optimization and calibration can make them relevant for 3D cell culture.

Paper ID 82

Antagonistic pharmacological interaction between cambinol and cisplatin in breast cancer model

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Background: Breast cancer (BC) is the most common cancer diagnosed among women worldwide. Despite numerous studies, the pathogenesis of BC is still poor understood and effective therapy of this disease remains challenge for medicine. Combined therapy of BC is considered as a promising anticancer tool leading to improve prognosis of BC patients and significantly decrease of adverse effects caused by standard chemotherapeutics. Sirtiun inhibitors are promising anticancer drugs, which inhibit proliferation of a wide variety of cancer cells including BC cells.

Aim: In the present study we investigated the influence of cambinol (CAM; sirtiun inhibitor), alone or in combination with cisplatin (CDDP), on proliferation, induction of apoptosis and cell cycle progression in MCF7, T47D, MDA-MB-231 and MDA-MB-468 BC cells. The type of pharmacological interaction between CAM and CDDP was determined by an isobolographic analysis. The isobolographic analysis is a very precise and rigorous pharmacodynamic method, to determine the presence of synergism, addition or antagonism between different drugs with using variety of fixed dose ratios.

Methods: Cell viability and proliferation assessments in BC cells treated with CAM, individually or in combination with CDDP, were performed by means of MTT and BrDU assays, respectively. The type of pharmacological interactions between CAM and CDDP was assessed using isobolographic method. The induction of apoptosis and cell cycle progression was determined using FACS analysis.

Results: Our experiments demonstrated that CAM suppresses the pro-apoptotic and anti-proliferative activity of CDDP, suggesting antagonistic interaction between these drugs. Isobolographic analysis confirmed that the combinations of CAM with CDDP at a fixed-ratio of 1:1 exerted antagonistic interaction in the viability of all analyzed BC cells.

Conclusions: CAM and CDDP used in combination produce antagonistic interaction, which may be a limitation in the use of these drugs in polytherapy. However, results obtained from *in vitro* studies should be thoroughly validated in *in vivo* models.

Paper ID 83

Hiding in plain sight : tryptophan metabolism in liver cancer

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Background: Although the liver is a site of robust immunological activity, liver cancer cells are able to remain undetected and proliferate. This suggests that these cancer cells have the ability to evade the local immune surveillance and kynurenine pathway (KP) of tryptophan metabolism, has been suggested to be one of the key mechanisms to mediate tumoural immune evasion. Despite accumulating evidence of the key roles of the KP in various cancers, little is known about the involvement of the KP in liver cancer and most, if not all, of the published literature are focused only on the first three enzymes of the pathway in liver cancer.

Aim: Our objective is to characterize the activity of the entire KP in liver cancer and examine whether KP activity measurement can be used as a prognostic biomarker to predict disease severity in liver cancer patients and/or a treatment target.

Materials & Methods: We examined the activity of KP in liver cancer by using established cell lines and clinical samples (n=30) obtained from untreated liver cancer patients using high-performance liquid chromatography (HPLC), ultra-HPLC and gas chromatography-mass spectrometry.

Preliminary results: We found that the activity of the upstream KP enzymes, indoleamine-2,3 dioxygenase (IDO1)/tryptophan-2,3-dioxygenase (TDO) and kynurenine 3-monooxygenase (KMO) were significantly elevated in liver cancer sera samples as compared to healthy control. While activity of the downstream KP enzyme, kynureninase (KYNU), was significantly lower in liver cancer sera. This suggests that KP activity in liver cancer is limited to the first two enzymes of the pathway and the immune evasion may be facilitated by the depletion of TRP and production of potent immune suppressive metabolites such as 3-Hydroxykynurenine (3HK).

Conclusion: KP is upregulated in liver cancer and KP profiling can be potentially used as a blood-based marker to predict disease severity in liver cancer patients and/or a treatment target.

Paper ID 84

Pattern of invasion in stage I Mucinous Ovarian Cancer is prognostic within 2-years of diagnosis

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Background: Mucinous Ovarian Carcinoma (MOC) is a rare epithelial ovarian cancer histotype. Over 80% are diagnosed at early stage (Stage I) with 5-year overall survival ~83%. The role of adjuvant chemotherapy in Stage I MOC is uncertain. Guidelines recommend chemotherapy in stage IC or higher, however prognostic biomarkers are lacking. A notable pathological feature in MOC is the pattern of

invasion (expansile or infiltrative). An infiltrative pattern is suggested to confer higher risk of relapse and mortality, however published series have been limited by small sample size.

Aim: To assess survival of patients with stage I MOC, comparing expansile and infiltrative pattern of invasion.

Methods: Samples and data from the Ovarian Tumor Tissue Analysis consortium were analysed. Haematoxylin and eosin-stained tumour sections were reviewed by expert gynaecological pathologists. Overall survival (OS) was estimated using Cox Proportional Hazards, with multivariable analyses adjusting for age and study site. OS was calculated from study entry to death or last known follow-up, and stratified by 0-2years vs. >2years.

Results: Pathology review confirmed 176 primary MOCs of which 133 were stage I, 83 IA, 1 IB, 37 IC, and 12 were I, unknown substage. Pattern of invasion was expansile in 109 (82%) and infiltrative in 24 (18%). There was no association with OS, (adjusted-HR 1.68 (0.72-3.94), p=0.23). After stratification at 2-years, a time-dependent difference was observed with a lower 2-year OS in the infiltrative subtype 70% compared to 86% in the expansile subtype (adjusted-HR 3.45 (1.12-10.68), p=0.03).

Conclusions: Patients with Stage I MOC and an infiltrative pattern of invasion had a higher risk of all-cause death within the first 2 years following diagnosis compared with the expansile pattern, reinforcing that this may be a consideration for selecting patients for adjuvant chemotherapy. Routine reporting of expansile/infiltrative subtype by pathologists is recommended to prospectively assess these findings.

Paper ID 85

A Unique Urinary Metabolomic Signature for the Diagnosis and Prognosis of Pancreatic Cancer

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Background: Pancreatic Ductal Adenocarcinoma (PDAC) continues to have poor survival outcomes. One of the major reasons for poor prognosis is the advanced stage of the disease at diagnosis. Hence, identification of a novel and cost-effective biomarker signature for early detection/diagnosis and prognosis of PDAC could lead to better survival outcomes.

Aim: Untargeted metabolomics was employed to identify a novel metabolite-based biomarker signature for PDAC diagnosis and prognosis.

Methods: Urinary metabolites from 92 PDAC patients (56 discovery cohort and 36 validation cohort) were compared with 56 healthy volunteers using ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectroscopy. Multivariate (Partial-least squares discriminate analysis) and univariate (Mann-Whiney's U-test) analysis were performed to identify a metabolite panel which can be used to detect PDAC. The selected metabolites were further validated for their diagnostic potential using the area under the receiver operating characteristic (AUROC) curve. Further, survival analysis was performed to determine the prognostic ability of identified metabolites.

Results: Statistical analysis identified a six-metabolite panel (trigonelline, glycolate, hippurate, creatine, myoinositol and hydroxyacetone) which demonstrated high potential to diagnose PDAC, with AUROC of 0.933 and 0.864 in the discovery and validation cohort, respectively. Notably, the identified panel also demonstrated very high potential to diagnose early stage (I and II) PDAC patients with AUROC of 0.897. Further, a panel of three metabolites (*i.e.,* trigonelline, hippurate and myoinositol) was able to stratify patients with good- or poor-prognosis based on overall survival. The PDAC patients with abnormal levels of 2 or more metabolites in their urine demonstrated significantly ($p < 0.05$) lower survival compared to patients with abnormal levels of one or less metabolites (median survival: 318 vs 564 days).

Conclusion: These results demonstrate that the selected metabolite signature could pave the way for the development of a urinary test for the early detection/diagnosis and accurate prognosis of PDAC.

Paper ID 88

Intermittent tumour hypoxia enhances HIF1A expression through histone demethylation

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Background: Chronic hypoxia is common in solid tumours and is associated with treatment resistance and aggressive disease. Intermittent hypoxia can also occur in tumours from fluctuations in perfusion and from sleep apnoea. Animal models of sleep apnoea show that intermittent hypoxia promotes tumour growth and metastasis. However, intermittent hypoxia is challenging to model *in vitro*, making it difficult to study the molecular mechanisms driving these changes. This includes oxygen-sensing pathways such as hypoxia inducible factor (HIF), which can promote tumour progression.

Aim: Our aim is to determine whether intermittent hypoxia activates HIF and other oxygen sensing pathways and if this impacts tumour cell behaviour.

Methods: Breast and colorectal cancer cells were exposed to chronic and intermittent hypoxia to mimic the *in vivo* tumour environment. Western blotting, qRT-PCR, ChIP-qPCR, tumour spheroids, and reporter gene assays were used to study changes in protein and mRNA expression and interactions with DNA.

Results and Conclusions: HIF-1α increases in tumour cells exposed to both chronic and intermittent hypoxia; however, HIF-1α is differentially activated depending on the type of hypoxia. In chronic hypoxia, HIF-1α is regulated in an oxygen-dependent post-translational manner, while in intermittent hypoxia, HIF-1α is regulated at the transcriptional level through histone H3K9 demethylation at the *HIF1A* gene. Demethylation of H3K9 at the *HIF1A* locus in intermittent hypoxia increases *HIF1A* mRNA expression, which has the downstream effect of increasing HIF-1 activity and expression of HIF-1 target genes associated with cancer progression. A 3-dimensional spheroid model incorporating both physiological chronic and intermittent hypoxia showed that intermittent hypoxia produces a stronger HIF response than with chronic hypoxia alone. This indicates that intermittent hypoxia may have consequences for tumour behaviour via activation of HIF.

Paper ID 89

Population pharmacokinetics of treosulfan in children receiving blood or bone marrow transplantation

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Background: Treosulfan is an alkylating agent administered intravenously to paediatric patients with malignant and non-malignant disease as part of conditioning therapy prior to blood or bone marrow transplantation. Cumulative treosulfan exposure (area under the curve; AUC) of 4800 mg*h/L has previously been identified as a target to maximise transplant engraftment success while minimising mortality in patients with immunodeficiency disorders. This target may not be indicative for patient populations with malignant or genetic disorders.

Aim: To develop a population pharmacokinetic model for treosulfan disposition in paediatric patients receiving treosulfan for malignant, immunodeficiency and genetic disorders.

Methods: 303 concentration data points were obtained from 46 patients (age 0.22 – 17; median 3.7 yrs) receiving 3 daily doses of treosulfan (30 - 42 g/m^2 cumulative dose) and analysed using nonlinear mixed effects modelling (NONMEM v7.4) software. Treosulfan clearance (CL) and volume (V) were assessed through different structural, error, covariate, and maturational models. Simulation-based visual predictive checks (VPCs) and non-parametric bootstrapping was performed for evaluation of model predictability and robustness (n = 1000).

Results: A one-compartment structural model with inter-individual variability on CL and V best described the data, and proportional and additive error terms described residual error. A weight-based covariate model, referenced at 70 kg, described both CL and V (15.60 L). CL was further evaluated across each day, with an allometric exponent of 0.75, and a sigmoidal maturation function using a fixed postmenstrual age of 40 weeks (7.07, 8.18, and 10.66 L/h, respectively). No model misspecification was observed based on goodness of fit plots, and bootstrapping and VPC parameters were acceptable. Comparison with trapezoidal-calculated AUC yielded strong correlation the model-calculated AUC (R^2 = 0.9579).

Conclusion: The model described treosulfan pharmacokinetics and variability well. Future directions are to perform a time-to-event analysis, correlating these findings with drug toxicity, engraftment success and event-free survival.

Translational significance: Providing a pharmacokinetic model for treosulfan in children with malignant or non-malignant disease will guide clinicians in providing the best dose to optimise clinical outcomes.

Paper ID 92

Being away from home for cancer treatment: qualitative study of patient experiences of SCN during RT

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Background: Supportive Care Needs (SCN) refers to support required by patients and their families to better cope with the burden of cancer. Many rural radiation therapy (RT) patients stay away from home for significant periods of time to attend for treatment. They have reported concern over travelling for RT, which can lead to the negative effects of both social isolation and cultural disparity. Patients often have a range of complex SCN and there is a lack of in-depth study of rural patient perspectives going through RT.

Aims: Explore and understand experiences of being away from home, consider patient perspectives of their own SCN and identify recurring themes. Give health professionals a deeper understanding of how these patients think and feel and provide a foundation of patient-centred insights for further research.

Methods: Thirteen patients participated in a face-to-face unstructured interview. All were staying away from home for RT at the North Coast Cancer Institute in Lismore for >three days-a-week for >three weeks. The data was subject to interpretive phenomenological analysis (IPA): a process of naive understanding and structural analysis followed by comprehensive understanding and reflection.

Results: Two themes which influenced patient experiences of their care; values and identity, and expectations. Patients discussed the value that they place on rural-life, community connections and healthcare. They referred to experiences of health service continuity and key information which helps manage expectations. SCN discussed fell into three categories; practical, physical and psycho-social.

Conclusions: Experiences of culturally appropriate patient-centred supportive care improve control and confidence as patients receive treatment away from home. Patient wellbeing is influenced by compassionate, caring and respectful connections with others. Several practical ways of better managing expectations and promoting the psycho-social wellbeing of these patients are supported. Future research can be shaped by insights from these lived-experiences.

Paper ID 94

Constitutive androstane receptor plays an important role in regulating liver cancer stem cells

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Background: We have observed that the constitutive androstane receptor (CAR) may play a critical role in human liver cancer development, specifically, in the regulation of liver cancer stem cells (LCSCs). Previous studies have demonstrated a hepato-protective for CAR in liver differentiation and regeneration. CAR has also been shown to regulate the function of human brain tumour stem cells (BTSCs) and inhibits the proliferation and expansion of BTSCs. The role of CAR in human liver cancer has not been defined.

Aims: To (***1***) investigate the role of CAR in human liver cancer; (***2***) investigate the regulatory role of CAR in liver cancer stem cells (LCSCs); and (***3***) clarify the CAR mechanism of action.

Methods: To study how CAR may exhibit a tumour suppressive role in human liver cancer, functional assays for migration, invasion and proliferation were undertaken in human liver cancer cell lines (Hep3B, Huh7 and PLC/PRF/5) treated with or without a CAR agonist, CITCO. LCSCs were enriched from cultured cells maintained under ultra-low attachment conditions for tumour sphere formation assays in the absence or presence of CITCO.

Results: Activation of CAR inhibited the proliferation of Hep3B ($p \leq 0.0001$), Huh-7 ($p \leq 0.05$) and PLC/PRF/5 ($p \leq 0.01$) cells. CAR activation significantly inhibited liver cancer cell migration (in Hep3B and PLC/PRF/5, $p \leq 0.05$; in Huh-7, $p \leq 0.01$) and invasion (in Hep3B, $p \leq 0.0001$; in PLC/PRF/5, $p \leq 0.01$). CAR activation inhibited tumour sphere formation in Hep3B cells ($p \leq 0.0001$) and this was associated with a significant reduction in CD44 expression ($p \leq 0.0001$).

Conclusion: CAR may play a tumour suppressive role in human liver cancer and may be an important regulator of LCSCs. Further studies are underway.

Paper ID 95

Generation and characterisation of liver specific Jagged2 knockout mice for liver cancer research

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Background: A thorough understanding of the molecular mechanisms responsible for the pathogenesis of liver cancer is essential for developing new therapies. We identified Jagged2 (Jag2) as a critical regulator for the tumorigenic ability of liver cancer cells and liver cancer stem cells. To obtain definitive confirmation on the role of Jag2 in the pathogenesis of liver cancer, we generated a conditional liver specific Jag2 knockout (LSJag2 KO) mice.

Aim: To generate and characterise the LSJag2 KO mice.

Methods: LSJag2 KO mice (C57 background) were generated by using Cre-Lox technology. Jag2 loxP "floxed" mice were crossed with Alb-Cre mice. The resultant mice were then crossed back with the Jag2 loxP "floxed" mice to generate LSJag2 KO mice (flox+/+ cre+) or flox+/+cre-(control). Genotyping for the Jag2 conditional allele was confirmed using PCR. Expression of Jag2 in tissues was determined by qPCR, Western blots, and immunohistochemistry.

Results: LSJag2 KO mice are healthy and active. No abnormalities were identified in key organs (liver, kidneys, lung, colon, stomach and heart). The impact of Jag2 deletion on the function of liver, kidney, and heart are underway. At the mRNA level, Jag2 was barely detectable in liver ($n=5$, $p<0.0001$) but expression in other organs was not altered ($n=5$, $p>0.05$). At protein level, no Jag2 was detected in liver ($n=3$, $p<0.0001$) but in other organs, Jag2 protein expression was comparable to that of control mice ($n=3$, $p>0.05$). Using immunohistochemistry analysis, Jag2 expression was barely observed in liver, but was present in other organs.

Conclusion: We have successfully deleted Jag2 in LSJag2 KO mice. This model will be a robust platform for investigating the role of Jag2 and Notch signalling in the pathogenesis of liver cancer.

Paper ID 98

Cannabidiol and Low-THC Cannabis Extracts for the Treatment of Acute Myeloid Leukaemia

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Background: Acute myeloid leukaemia (AML) is the most common subtype of acute leukaemia and one of the most lethal of all cancers. In Australia annually, 900 patients are diagnosed with AML, with 800 patients succumbing of their disease. New non-toxic therapeutics are desperately needed for these high-risk patients. Cannabis has been used medicinally for thousands of years. The major non-psychotropic cannabinoid, cannabidiol (CBD), makes up >60% of low-Delta-9-tetrahydrocannabinol (Δ^9-THC) containing cannabis, and is entering the Australian market as a 'complementary therapeutic'.

Aim: To determine whether low-THC cannabis extract (CE) or CBD alone or in combination with cytarabine (Ara-C) has anti-AML potential.

Methods: Resazurin growth and proliferation, Annexin/V cell death and clonogenic assays using AML cell lines (n=5) *in vitro*, patient samples (n=3) *ex vivo* and CD34+ normal bone barrow (NBM) cells were treated with CE, CBD and THC. We also employed the MV4-11 derived xenograft mouse model to test therapies *in vivo*.

Results: CE (mean IC_{50} 3.9µg/mL) and CBD ($\bar{x}$ IC_{50} 4.3µg/mL) were cytotoxic to AML cell lines independent of recurring mutations, while non-toxic to CD34+NBM. Combination of CBD with Ara-C showed additive cytotoxicity (IC_{50}: CBD 2.1uM, Ara-C 1.7uM). AML patient samples *ex vivo* were highly sensitive to CBD (1.5µg/mL +/-) and Hemp (6ug/mL +/-). CBD alone extended survival of AML xenograft mice compared to vehicle control (p=0.0004), as did CE when combined with Ara-C (p=0.0132). Mechanistic studies identified agonism of the peroxisome-proliferator-activated receptor alpha (PPARα) by CBD, activating E3 ubiquitin ligase driving degradation of the antiapoptotic protein BCL2 and driving cell apoptosis**.**

Conclusions: Non-psychoactive cannabinoids show encouraging anti-AML activity. Work continues to validate results using knockdown models. However, significant pharmacology is required to optimise beneficial formations.

Translational Aspect: This study provides the basis for driving this paradigm towards phases I/II clinical trials.

Paper ID 101

Acute disseminated intravascular coagulation - a rare presentation of occult large cell carcinoma

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Background: Disseminated intravascular coagulation (DIC) is a haematological phenomenon that can be acute or chronic in nature and is characterised by bleeding and/or thrombosis. Large cell carcinoma is a neuroendocrine malignancy that is usually associated with a pulmonary predominance, however the disease itself is not confined to the thorax with multiple organ systems having previously been implicated. There is scarcity in the literature with regard to the association of large cell carcinoma with acute DIC.

Aim: We present the case of a 43-year-old male who presented to our institution with flank pain who was subsequently diagnosed with acute DIC secondary to metastatic undifferentiated large cell carcinoma.

Results: A 43 year old male presented to a metropolitan emergency department with lethargy and right flank pain. On clinical examination he was tachycardic, tachypnoeic and hypoxic requiring supplemental oxygen therapy. Splinter haemorrhages and lower limb purpura was present while thoracic examination revealed widespread coarse crepitations. Assessment of his back revealed tenderness over the midline at the level of L2. Biochemical assessment revealed a lactate of 5.8 mmol/L, along with significant hypercalcaemia (3.55 mmol/L) and thrombocytopenia. Further to this he was coagulopathic with an INR of 1.8 and PT of 23.5 seconds. His D-dimer was significantly elevated to 19.97 mg/L. CT thoracolumbar spine revealed an L2 fracture, while CT kidney, ureter and bladder demonstrated para-aortic lymphadenopathy, peritoneal nodules, and low-density hepatic lesions concerning for metastatic foci. The patient required admission to the intensive care unit, with subsequent ultrasound guided biopsy of the left lobe of the liver demonstrating metastatic large cell undifferentiated carcinoma of the pancreatico-biliary tract and upper gastrointestinal tract. The patient progressed to multi-organ failure requiring non-invasive ventilation and haemodialysis, and died four days post presentation.

Conclusions: This case highlights a rare presentation of metastatic undifferentiated large cell carcinoma and provides further evidence for the association of acute DIC with solid organ malignancies, as well as reaffirming the poor prognosis associated with acute DIC.

Paper ID 102

Association of microRNAs and adipokines in the serum of breast cancer survivors with arm lymphedema

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Introduction: Arm lymphedema is major challenge faced by breast cancer survivors following breast cancer treatment. It is characterized by lymphatic fluid retention and swelling in one or both arms that arises after obstruction of lymphatic vessels. Providing that the condition is multifactorial, the characterization of microRNAs and adipokines may lead to the discovery of novel biomarkers involved in pathological conditions of lymphedema.

Objective: This study aimed to identify circulating microRNAs and adipokines in the serum of breast cancer survivors that could serve as potential biomarkers associated with breast cancer-related lymphedema.

Methods and results: A total of 113 breast cancer survivors were recruited and the inclusion criteria were being female, aged >18, no current of evidence of cancer and all treatments completed >3 months prior to recruitment. Blood was collected and processed to obtain serum for small RNA-sequencing (lymphedema vs non-lymphedema, with n=7 each group). MiRNAs that were differentially expressed (fold change >1.5, $p< 0.05$) between cases with lymphedema compared to those without lymphedema were validated in a second cohort, through quantitative PCR (lymphedema n=16, non-lymphedema=83, normalized to miR-16-5p as endogenous control). The leptin and adiponectin levels were measured using ELISA method (lymphedema n=22, non-lymphedema = 86). Two of the most significantly upregulated microRNAs, miR-199a-3p and miR-151a-3p were revealed to be strongly correlated with hypertension and diabetes in the lymphedema group. Leptin levels were higher in the lymphedema group regardless of the body mass index classes (<25 kg/m^2 or >25 kg/m^2) when compared to the non-lymphedema group ($p< 0.05$). Meanwhile, no significant difference was observed in adiponectin levels between the two groups ($p = 0.09$).

Conclusions: miR-199a-3p and miR-151a-3p may serve as candidates to predict the onset of lymphedema in breast cancer survivors with underlying hypertension and diabetes. Meanwhile, extensive studies on the mechanisms of leptin association with arm lymphedema is necessary to provide new insights for the search of lymphedema biomarkers.

Paper ID 103

Economic evaluation of breast and ovarian polygenic risk scores for women with a pathogenic variant

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Background*:* Polygenic risk modifies breast and ovarian cancer risk in carriers of moderate and high-risk rare pathogenic variants (PV). The addition of a polygenic risk score (PRS) to genomic risk assessments would facilitate more personalised risk estimates and risk management advice, but the effectiveness of this approach is unknown.

Aim*:* Estimate the long-term clinical and cost-effectiveness outcomes of a genomic risk assessment including a PRS for breast and ovarian cancer for carriers of PV in high/moderate-risk genes using microsimulation.

Methods*:* A validated simulation model (miBRovaCAre) was adapted to include a PRS. The target population was cancer-unaffected women aged 20-39 years, with a PV (genes included *BRCA1/BRCA2/PALB2/ATM/BRIP1/CHEK2/RAD51C/RAD51D)*. Using accepted 10-year and lifetime risk management thresholds, the intervention was incorporation of a PRS to determine uptake and timing of risk management strategies, compared to current practice (based on the PV alone).

Results*:* Introducing a PRS resulted in 0.16 quality-adjusted life-years saved per carrier at an average additional cost of $AUD1454, likely representing a cost-effective addition to current care. In general, the greatest benefit was seen in women in the highest quintile for PRS (breast and/or ovarian). An important contribution arose from improved personalisation of the recommended age for risk-reducing salpingo-oophorectomy (RRSO). In women in the highest quintile of the PRS the estimated average age of RRSO was reduced from 42.05 under current practice to 37.16 years by addition of the PRS.

Conclusion*:* Tailoring cancer risk management through personalised germline risk assessments with a PRS could greatly benefit moderate- and high-risk PV carriers.

Paper ID 105

Targeting Ferroptosis in Glioma Stem Cells to Prevent Drug-Resistance and Recurrence of Glioblastoma

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Background: Glioblastoma (GBM) is the most lethal form of adult brain cancer, with < 5% of patients surviving past 5-years following diagnosis. GBM are heterogeneous tumours composed of a small population of glioma stem cells (GSCs), which exhibits high tumourigenicity. GSCs are linked to recurrence and drug-resistance, which are a hallmark of highly aggressive drug-resistant brain cancers. GBM patients' are currently treated with the Stupp protocol, which includes surgical resection, followed by radiation and temozolomide (TMZ). As the administration of chemotherapeutics/radiation occurs in cycles, to allow patient recovery, this also provides an opportunity for regrowth of drug-resistant tumours and the phenotypic shift of non-GSCs to GSCs. Currently, no clinical treatments are available for GSCs.

Aim: Our aim was to examine whether GSCs in GBM can be eradicated by ferroptosis, which is a non-apoptotic-regulated mechanism of cell death.

Methods: This study utilized GBM cell lines, U87MG-Parental and U87MG-TR (Temozolomide-resistant) cells to elucidate if ferroptosis can inhibit GSCs resistance and recurrence. Cell lines were treated with: ferroptosis inducers (i) RAS-selective lethal molecule 3 (RSL3; inhibitor of glutathione peroxidase; GPX4); or (ii) erastin (inhibitor of System X^-_c transporter); while (iii) liproxstatin-1 (Lip-1) was used to reverse the ferroptotic process. Expression of resistance/GSCs/ferroptosis markers was measured by western blotting. Resistance/stemness-phenotype was determined by viability assay (MTT) and neurosphere-formation (Elispot).

Results: Our preliminary studies demonstrated that induction of ferroptosis (observed by decreased GPX4 and System X^-_c transporter levels) decreased CSCs markers, cell viability and regrowth of GBM neurospheres, while LIP-1 was found to reverse ferroptosis, by increasing cell viability/regrowth of temozolomide-resistant U87MG-TR cells. Ferroptosis inducers were also found be more effective at eradicating U87MG-TR than U87MG-Parental cells.

Conclusion and Translational potential: The induction of ferroptosis is a promising strategy for targeting drug-resistant GSCs that drive recurrence of GBM tumours.

Paper ID 106

Herpes Zoster re-activation in combination chemoimmunotherapy: case report

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Background: Although immunomodulatory medications are known to increase the risk of re-activation of herpes zoster virus, there are few literature cases published describing the link between anti-programmed cell death ligand 1 inhibitors and cutaneous reactivation.

Case: We present a 66-year-old man who was undergoing combination chemoimmunotherapy with carboplatin, etoposide and atezolizumab for extensive stage small cell lung cancer. Within 7 days of completing his first cycle, he developed a maculopapular, erythematous, pruritic cutaneous reaction on his left lateral flank in the T7 dermatomal distribution. He had no prior history of shingles infection and did not recall any specific history of varicella as a child. Histopathology of a punch biopsy described acantholysis and keratinocytes within the lesion consistent with varicella zoster shingles infection. He was treated with a 7-day course of valaciclovir with good effect. In terms of his ongoing progress, there have been case reports of post-shingles granulomatous dermatosis within the same dermatomal distribution related to anti-PDL/PDL1 treatments and this is a concern for him in future.

Discussion & Conclusion: Our case report is important in the context of dermatological complications of immunotherapy. HSV re-activation is a known chemotherapy complication and with the widespread use of immunotherapy and chemotherapy combinations in multiple tumour streams, oncologists need to be aware of both the risks of HSV re-activation as well as post-shingles granulomatous syndromes. Current case reports suggest that these reactions are moderate in severity with no reports requiring permanent immunotherapy discontinuation. Furthermore, epidemiological studies into the extent of HSV re-activation in the chemoimmunotherapy setting would be useful to determine the risk of recurrence and its associated morbidity.

Paper ID 108

DBT and ultrasound in the evaluation of mammography-recalled women with dense and non-dense breasts

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Background: DBT and ultrasound might overcome some of the limitations of 2D digital mammography for detection of breast cancer across dense and non-dense breast.

Aim: To evaluate the diagnostic performance of adjunctive DBT in comparison to ultrasound in women recalled for additional imaging due to digital mammographic findings.

Methods: A total of 482 patients (mean age: 59.3; SD: ± 8.8 years) recalled for DBT and ultrasound from January 2017 to December 2019 were included in this study. Women met the inclusion criteria if they had undergone both DBT and ultrasound and had confirmed biopsy results. We calculated the sensitivity, specificity, ROC AUCs, and false-positive rates for DBT and ultrasound across dense and non-dense breasts.

Results: A total of 296 breast cancers (232 invasive, 64 non-invasive) were detected. In dense breasts, DBT showed significantly higher sensitivity than ultrasound (98.2% vs 80%; $p < 0.001$), but significantly lower specificity (15.4% vs. 55%; $p < 0.001$) and AUC (0.568 vs 0.671; $p = 0.001$), compared with ultrasound. In non-dense breasts, no significant differences between DBT and ultrasound in specificity (22% vs. 33%; $p = 0.14$) or AUC (0.606 vs. 0.583; $p = 0.57$). However, the sensitivity of DBT was also significantly higher than that of ultrasound (99.2% vs. 84%; $p <0.001$). For women recalled due to the presence of calcification in their mammograms, ultrasound showed significantly better AUC than DBT in dense breasts (0.647 vs 0.509; $p < 0.001$), but no significant difference in non-dense breasts (0.630 vs 0.500; $p = 0.15$). DBT showed significantly higher false-positive rate than ultrasound in dense breasts (84.6% vs 45%; $p < 0.001$), but no significant difference in non-dense breasts (78% vs 67%; $p = 0.14$).

Conclusion: In mammography-screened women recalled for additional imaging, DBT detects more breast cancers but results in significantly higher false-positive rates than ultrasound, particularly in dense breasts.

Paper ID 109

Liquid Biopsy to Assess Clonal Architecture and Evolution in Diffuse Midline Glioma in Real-Time

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Background: Recent whole-genome profiling studies have revealed a high degree of intra-patient genomic heterogeneity in Diffuse Midline Glioma (DMG), highlighting why mono-therapeutic treatment strategies fail, and median overall survival remains 11 months post-diagnosis.

Aim: This raises the question, whether we can monitor tumour evolution in real-time to determine why experimental treatments fail and guide novel therapies?

Methods: We tested this hypothesis using a 30x whole-genome sequencing approach on cell-free DNA (cfDNA) donated from a DMG patient receiving the experimental treatment, ONC201. We identified the same *PIK3CA* mutation (E545A) in cfDNA that was present at diagnosis in tumour tissue (PRISM). This encouraged us to optimise a high-throughput Illumina TruSight Oncology 500 (TSO500) panel at a sequencing depth of 2500x for patient cfDNA and matched autopsy samples.

Results: TSO500 sequencing of cfDNA from a DMG patient identified numerous, clinically relevant, mutations. When compared to next-generation sequencing data from a matched autopsy sample, there was a notable overlap in the mutations present in both samples. Filtering for missense variants only, 179 single nucleotide variants (SNV) were identified within the autopsy sample while 143 SNVs were identified in cfDNA which was obtained prior to patient relapse. We are now investigating the potential of utilising cfDNA to determine tumour clonal architecture and evolution. Work continues to identify subclones and potential driver mutations present within autopsy tumour samples and assess whether cfDNA can produce the same results.

Conclusions: Our liquid biopsy pipeline could allow for the real-time subclonal genomic analysis of patients with CNS malignancies. Tumour clonal architecture may be assessed at diagnosis and used to

guide initial treatments, then progressively examined throughout therapy to monitor treatment-induced subclone and driver mutation changes. Coupled with cfDNA as a less invasive source of genomic information, this approach has the potential to provide DMG patients with more favourable outcomes.

Paper ID 110

Assessment of HR deficiency in ovarian cancer to increase PARP inhibitor targets beyond BRCA1/2

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Background: PARP inhibitor (PARPi) maintenance treatment following primary chemotherapy is now the standard of care for ovarian cancer patients with pathogenic *BRCA1/2* variants. Consequently, *BRCA1/2* testing is becoming part of the treatment algorithm to identify women who will benefit from a PARPi. However, alterations in additional genes resulting in homologous recombination DNA repair deficiency (HRD) may also predict PARPi response, potentially increasing the number of patients who may benefit.

Aim: To determine global HRD status and association with HR pathway genealterations in prospectively recruited ovarian cancer patients.

Methods: Women with epithelial ovarian, fallopian tube or peritoneal cancer were recruited to INOVATe (Individualised Ovarian Cancer Treatment through Integration of Genomic Pathology into Multidisciplinary Care) and tumour testing performed at diagnosis and/or at relapse. Multi-gene targeted sequencing was performed and HRD status was predicted by an HRD assay score based on a combination of three genomic features from whole genome single nucleotide polymorphism array data: Telomeric Allelic Imbalance, Loss of Heterozygosity and Large-Scale Transition. *BRCA1* and *RAD51C* methylation were assessed by methylation-specific high-resolution melting.

Results: Mutation testing in 333 women with high-grade serous carcinoma (HGSC) identified pathogenic alterations in *BRCA1/2* in 85/333 (25.5%), with 56/333 (16.8%) shown to be germline mutations. HRD score was determined in 123 HGSC cases with more than half predicted as HR deficient (70/123, 57%). *BRCA1/2* mutations were found in 31/70 (44%) of HR deficient cases. Of the 39 *BRCA* wild-type/HR deficient tumours, alternate mechanisms underlying HRD have so far been found in 27 cases (69%): *BRCA1* methylation (n=20), *RAD51C* methylation (n=3), and mutations in *BARD1*, *BRIP1* or *PALB2* (n=4).

Conclusion: Use of a global HRD score assay effectively identified HR-deficient HGSC in the context of both mutant- and wild-type *BRCA1/2*. This may predict response to PARPi, potentially increasing their use in clinical practice.

Paper ID 113

The cost-effectiveness of tailored colonoscopic surveillance strategies for Lynch syndrome carriers

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Background: The lifetime colorectal cancer (CRC) risk in individuals with Lynch syndrome (LS), a hereditary cancer predisposition syndrome, substantially varies by mismatch repair (MMR) gene. However, there is limited evidence of the effectiveness of MMR gene-specific colonoscopic surveillance.

Aim: This study aims to evaluate the health impact and cost-effectiveness of tailored colonoscopic surveillance strategies for LS carriers by MMR genes (*MLH1*/*MSH2*, *MSH6* and *PMS2*).

Methods: We first estimated sex- and MMR gene-specific cumulative risk of first CRC without colonoscopic surveillance using an optimisation algorithm. We then used the CRC risk estimates in a microsimulation model '*Policy1-Lynch'* to model ongoing colonoscopic surveillance in confirmed LS carriers. A total of 126 surveillance strategies, comprising combinations of start age, end age and surveillance interval, were compared against no surveillance.

Results: Considering all strategies: i) starting surveillance at age 25, rather than 20, was more cost-effective without changing life years saved (LYS) and starting 5-10 years later for *MSH6/PMS2* carriers further improved the cost-effectiveness; ii) surveillance end age (70, 75 or 80) had a relatively minor effect; iii) 3-yearly surveillance strategies were more cost-effective than 1 or 2-yearly surveillance strategies but prevented 3 fewer CRC deaths/1,000 LS carriers; and iv) less intensive surveillance after age 60 had minimal impact on LYS but less intensive surveillance up to age 40 resulted in substantially fewer LYS. Accordingly, the most cost-effective strategy was 3-yearly surveillance from 25-70 (*MLH1*/*MSH2*) with delayed surveillance for *MSH6* (age 30-70) and *PMS2* (age 35-70) carriers (incremental cost-effectiveness ratio: A$8,833/life-year saved). Compared to no surveillance, this strategy averted 60 CRC deaths and involved 9,206 colonoscopies (153 colonoscopies/death averted) over the lifetime of 1,000 confirmed LS carriers.

Conclusion: This is the first formal evaluation of MMR gene-specific colonoscopic surveillance. We found that a tailored approach would be effective and cost-effective. Ongoing emerging data will reduce the uncertainty of the lifetime risk estimates and inform ongoing discussions around optimal surveillance.

Paper ID 114

Combination of Paxalisib and ONC201 for the Treatment of Diffuse Intrinsic Pontine Glioma

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Background: Diffuse intrinsic pontine glioma (DIPG), is a highly aggressive, childhood brain cancer with a median overall survival of 9-11 months. Remarkably, 80-90% of patients harbour a recurring point mutation in histone H3 encoding genes, resulting in a lysine-to-methionine substitution (H3K27M). Recent clinical reports in DIPG have shown that ONC201 increases survival by ~6 months, however patients invariably become resistant or do not respond to treatment.

Aim: To improve response to ONC201 treatment.

Methods: Using H3K27M patient derived DIPG cell lines, ten of thirteen responded to ONC201 treatment. Quantitative proteomics was performed on the ONC201 resistant line, SU-DIPG-VI, +/- ONC201 to determine mechanisms of resistance.

Results: Pathway analysis of proteomic profiling revealed that cells treated with ONC201, upregulated the AKT signalling pathway. ONC201 is a known agonist of CLPP, degrading SDHA, leading to mitochondrial dysfunction, therefore ONC201 resistance may be driven by reprogramming to anaerobic glycolysis, underpinned by PI3K/AKT. To exploit this therapeutic vulnerability, we utilised the blood-brain barrier permeable PI3K inhibitor, paxalisib, currently in clinical trials (NCT03696355) in combination with

ONC201. *In vitro* combination treatment induced synergistic cell death in both ONC201 sensitive and resistant H3K27M DIPG cell lines. To confirm the clinical utility of this combination, we examined the efficacy of ONC201 and paxalisib in a SU-DIPG-VI, H3K27M DIPG, patient derived orthotopic xenograft model. ONC201 (p=0.01) and paxalisib (p=0.01) both increased overall survival as monotherapies. However, in combination, ONC201 and paxalisib and induced a significant synergistic effect on overall survival (p=0.0043).

Conclusions: These data highlight the clinical and therapeutic promise of the combination of ONC201 and paxalisib.

Paper ID 116

The estimated impact of COVID-19 on Australia's BreastScreen Program

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Background: Health services in Australia have been directly and measurably affected by the COVID-19 pandemic including disruptions to the delivery of its national breast screening program (BreastScreen). Simulation modelling offers a way of estimating the potential impact of the COVID-19 pandemic on population-level breast screening.

Aim: To evaluate how national-level pauses to the BreastScreen Australia (BSA) program would impact on cancer outcomes compared to no disruption of the BSA program.

Method: Policy1-Breast is a continuous-time, multiple-cohort micro-simulation whole-population model incorporating breast cancer risk, breast density, menopause, hormone therapy use and breast cancer screening. We used Policy1-Breast to model the effect of 3 hypothetical disruption scenarios, a 3-, 6- and 12- month pause to BreastScreen services in Australia. Estimated clinical outcomes included interval cancer rates, tumour size at detection, and breast cancer survival. Client prioritisation protocols were introduced to give higher priority to screen specific groups of women following resumption of services.

Results: We estimated that a 3 month pause in the screening program would decrease screen-detected cancers by 11% and reduce the proportion of diagnosed small-size cancers by 1% in women aged 50-74 over a period of 12 months following the pause. For subsequent round screening, the median time since the prior screen would be extended by up to 6.5 months (28 weeks), potentially leading to an increase in interval cancer rates. Furthermore, we estimate a reduction by more than 1% in 5-year survival after diagnosis for women who were due to screen in the first 12 months after the start of the disruption. Longer pauses are estimated to have more significant effects.

Conclusions: This modelled evaluation demonstrates the possible short and longer-term effects of a COVID-19 induced pause in the program. As BreastScreen participation data for 2020-21 becomes available, we will adapt our model to produce more refined estimates.

Paper ID 117

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 characterise 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.

Paper ID 119

cMet signaling affects the invasive capacity of a gastric cancer cell circulating tumour cell line

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Background: Gastric cancer is among the deadliest of adult cancers worldwide. Patients often present with advanced-stage cancer as early disease is usually asymptomatic. Liquid biopsies have given researchers a new understanding of the transitional biology of circulating tumour cells (CTCs) that have escaped the primary tumour on their way to form metastases. Capturing and investigating CTCs has provided insight into tumour cell behavior and recurrent disease prediction; e.g. via the analysis of mutated genes that are vital for cell migration, invasion or cell death. The tyrosine kinase, cMet, and the phosphatidylinostitol 3-kinase, PI3K, are key signaling proteins in these processes and are often mutated in cancer.

Aim: To identify unique and/or common pathways utilized for invasion and migration by our established CTC line (UWG02CTC) derived from a patient with gastroesophageal cancer.

Methods: We used 3D organotypic invasion models, cell proliferation and western blot assays with selective stimulating and inhibitory molecules of the cMET and PI3K/AKT pathways, to investigate the effects of these signaling pathways on CTC invasion and phosphorylation status.

Results: UWG02CTCs carry a gain-of-function mutation in the cMet receptor as well as in the catalytic subunit of *PI3K*, *PIK3CA*. Consequently, these pathways were constitutively activated. Treatment with HGF did not significantly enhance invasion though a transient inhibition of the PI3K/AKT and MAPK pathways was observed suggesting potential signaling cross-talk. cMET inhibitor AMG337 had no effect on cell proliferation but significantly inhibited invasion.

Conclusions: cMet and PI3K may communicate through interlinked signaling pathways to alter cell migration and invasion potential; further investigations are required to pin-point inter-pathway connections and the impact of *MET* and *PIK3CA* mutations on cell migration in our 3D model. Our work demonstrates the unique insights of tumour biology provided by CTC lines.

Paper ID 121

SWATH-MS protein profiling of plasma extracellular vesicles determines markers for GBM progression

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Introduction: Glioblastoma (GBM) is the most common and severe adult primary brain tumour. GBMs recur quickly and acquire more aggressive characteristics, and current monitoring methods lack the sensitivity to accurately detect GBM progression. A liquid biopsy that measures GBM molecules in the blood could enable tumour evolution to be monitored in real-time and allow for early tumour changes to be detected before patients become symptomatic. In this regard, circulating extracellular vesicles (EVs) are promising biomarkers that are readily accessible from the blood of GBM patients. EVs are 30-1000 nm membrane particles that are secreted by all cells, and are ideal biomarkers as they carry molecules (DNA, RNA, protein and lipids) that reflect the identity of their cell-of-origin. Despite their suitability, the complexity of the blood hinders in-depth mass spectrometry characterisations of circulating-EV proteins.

Aim: Using a data-independent acquisition (DIA) mass spectrometry (MS) platform, SWATH-MS, we aimed to comprehensively profile GBM plasma-EV proteomes and determine circulating-EV protein signatures that reflect GBM tumour burden.

Method: EVs were isolated by size exclusion chromatography from the plasma of 35 GBM patients at multiple time points over the course of their tumour (pre-operative, post-operative and recurrence; *n*=81), metastatic brain tumours (*n*=21) and healthy controls (n=22). Nanoparticle tracking and transmission electron microscopy confirmed the isolation of small-EV subtypes (< 200 nm). The plasma-EV peptides were sequenced by SWATH-MS, and protein identities and quantities were extracted using a spectral library comprised of 8662-protein species.

Results: A total of 3278 proteins were identified in plasma-EVs. Significantly changing proteins across the GBMs and controls ($p < 0.05$) included proteins previously reported to have significance in GBM-EVs. PCA showed excellent discrimination between the patient cohorts and plasma-EVs resampled at recurrence grouped with more aggressive samples.

Conclusion: Using SWATH-MS we have comprehensively profiled GBM plasma-EV proteomes and showed that plasma-EV markers can predict GBM tumour progression. Determining a set of circulating-EV proteins that can stratify GBM patients and predict recurrence, progression and treatment resistance, has great potential to enhance patient care.

Paper ID 123

Plasma extracellular vesicles for brain tumours diagnostic and disease progression monitoring

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Background: Glioblastoma multiforme (GBM) is one of the deadliest brain tumours in adults, with a short survival time. The most common diagnosis and disease progression monitoring are imaging based techniques, that are laborious. There is a need for a more specific, sensitive, and simple detection method, such as blood-based biomarkers, that would highly benefit the GBM patients and clinicians. The blood and other bodily fluids contain circulating extracellular vesicles (EVs), released by healthy and tumour cells, with specific genetic material content that can have clinical value.

Aim: Develop a robust and efficient blood-based biomarker for diagnostic and disease progression monitoring for brain tumours.

Methods: EVs were isolated with size-exclusion chromatography from GBM patients and healthy controls plasma and characterized based on their shape, size, and surface protein expression. Total RNA was extracted from the isolated EVs and deep sequencing was performed for the detection of small RNAs. Data analysis and bioinformatics tools were applied for the identification of differentially expressed miRNAs that have biomarker potential.

Results: Several significant differentially expressed (DE) microRNAs (miRNAs) were identified between GBM and healthy subjects. Some of these miRNAs, such asmiR-485-3p and miR-486-5p have been previously detected as up-regulated in GBM patient's serum and neurosurgical EVs. Furthermore, these two miRNAs and other DE miRNAs were found to distinguish metastatic GBM patients from primary GBM patients. DE miRNAs that reflect the tumour burden were also detected.

Conclusions: Plasma EVs small RNA content have possible diagnostic and disease progression monitoring values in GBM patients.

Translational significance: The validation and introduction in clinical settings of these biomarker candidates, would contribute to a more time efficient accurate diagnosis and disease progression monitoring. It could also play an important role in treatment plan decision.

Paper ID 124

Targeting NADPH Oxidases Improves Response to FLT3 Inhibitors for the Treatment of AML

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Background: Reactive oxygen species (ROS) are crucial regulators of cell signalling via their ability to oxidise enzymes at cysteine residues. ROS driven oxidative stress is a hallmark of acute myeloid leukaemia (AML), driving genomic instability, clonal evolution and treatment resistance. However, proteins influenced by ROS-induced Redox reactions remain unknown.

Aim: To characterise the Redox proteome of primary AML patient samples to identify novel treatment targets to increase response to clinically relevant therapies.

Methods: Cysteine oxidised proteins enriched from primary AML patient samples were characterised by Redox profiling. The therapeutic potential of targeting Redox sensitive proteins was assessed using experimental and clinically relevant inhibitors. Patient-derived AML cells were engrafted into NSG mice and treated with novel ROS inhibitors alone and in combination with sorafenib or midostaurin. Redox proteomics was performed on bone-marrow cells harvested from xenograft mice and assessed by Redox profiling.

Results: FLT3-mutant patients showed increased cysteine oxidation in the Src-family kinases and the NOX2-complex which is directly responsible for ROS production. Targeting NOX2 (inhibitors/siRNA) significantly decreased oncogenic signalling and was synergistically cytotoxic when combined with FLT3-inhibitors. Inhibition of NOX2 in AML xenograft models increased survival as a monotherapy. NOX2-inhibitors combined with FLT3-inhibitors increased overall survival compared to monotherapies. Redox proteomics in AML cells harvested from the bone-marrow of xenograft models revealed NOX2-inhibition decreased total NOX2 expression leading to decreased FLT3 signalling through reduced oxidation of FLT3-Cys828. Subsequent analysis of signalling pathways downstream of FLT3 revealed decreased activity of the key growth and survival factors STAT5 and ERK.

Conclusion: Using a clinically relevant NOX-inhibitor we are revealing the clinical relevance of targeting ROS production for the treatment of AML.

Paper ID 127

Moral Distress within Oncology: A Systematic Review.

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Background: There is growing clinical and ethical complexity within oncology and correlations between moral distress and factors prevalent among healthcare professionals (HCPs) in oncology, suggesting prevalence of moral distress among HCPs within oncology. This, alongside the increasing interest of moral distress within health care, warrants consolidation of what is known about moral distress within oncology.

Aim: This study systematically synthesised findings from research about moral distress among HCPs within oncology to inform future avenues of moral distress research and interventions.

Methods: Medline, EMBASE, PubMED, Scopus, PsycINFO, PsycARTICLES, and CINAHL databases were searched based on key word and MeSH terms 'moral distress', 'health care professional', and 'oncology'. Data from studies reporting on moral distress among HCPs in oncology, published in English up to August 2020 were included. Quality of articles were assessed with the Critical Appraisal Skills Program Checklists (CASP). The review was preregistered with PROSPERO (ID#200273) and adhered to PRISMA guidelines.

Results: Of 1282 articles identified, 33 were retained for data extraction. Articles where qualitative (n = 17), quantitative (n = 13), and mixed (n = 3) designs and primarily from the U.S.A. (n = 15) or Europe (n = 12). A range of definitions, measures, and comparators of moral distress were identified. Meta-synthesis identified five themes: (1) Communicating Conflicting Values, (2) Hierarchy and Power, (3) Violation of 'Do No Harm', (4) Impact of Moral Distress, and (5) Managing Moral Distress. Most studies presented the majority of details asked of CASP Checklists, although of low quality. Future avenues for interventions to mitigate moral distress within oncology were identified.

Conclusions: This systematic review is the first to map the experience of moral distress in oncology and analyse the relationship between moral distress and other constructs among cancer care professionals. The review highlights the constructs associated with moral distress, implications for clinical practice, and suggestions for interventions to minimise moral distress.

Paper ID 128

Predictive immune signatures in peripheral blood of patients undergoing checkpoint inhibitor therapy

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Background: Monoclonal antibodies targeting the Programmed death-1 (PD-1) axis are now routinely used in clinical practice. However, identifying cancer patients who will derive clinical benefit remains a key challenge. Previously, our group discovered a unique immune signature that distinguishes responders from non-responders with the highest accuracy so far achieved. This signature encompasses deficits in a number of T and NK cell populations. We hypothesised that this signature may be due to tumour-dependent systemic effects on the T-cell receptor zeta chain (TCR ζ, CD247) that is expressed in all T-cells and the majority of NK cells and is required both for cell survival and response to tumour.

Aim: To test correlations between expression of CD247, the immune signature and clinical response in cancer patients treated with agents targeting the PD-1/PD-L1 pathway.

Methods: Peripheral blood mononuclear cells from cancer patients undergoing PD-1 blockade were isolated before the first and second treatment cycles. Clinical response based on RECIST criteria was determined at 3 months. High dimensional phenotyping via flow and mass cytometry was conducted. Following manual gating of populations of interest, significance analysis of microarrays (SAM) analysis was used to identify signatures that correlated with clinical response, with subsequent analysis of CD3 and CD247 expression via signal intensity.

Results: Non-responders exhibited decreased percentages of lymphoid cell populations including effector and memory T-cell populations and increased percentages of myeloid lineages including monocytes, as compared to responders and healthy controls. SAM analysis highlighted increased proportions of regulatory T-cells and decreased proportions of inflammatory monocytes in non-responders. Moreover, non-responders also exhibited lower CD247 expression on multiple T-cell subsets but not in myeloid subsets.

Conclusions: These results indicate that decreased CD247 expression is correlated with deficits in the cellular arm of the adaptive immune response in non-responders to PD-1 blockade. This study may lead to the future implementation of a highly accurate prognostic tool in checkpoint inhibitor therapy.

Paper ID 129

PROSPER: Proliferation Signature in Prognosticating ER+ breast cancer

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It is recognized that breast cancer is not one disease, but a heterogeneous group that can be classified into clinically different subtypes, based on histopathological and molecular features. Breast cancers can be categorised into different subtypes with varying clinical outcomes, based on their gene expression profiles. Estrogen receptor positive (ER+) breast cancer is classified into two intrinsic molecular subtypes: luminal A and luminal B. Outcomes are overall poorer in the luminal B subtype in which proliferation rates are overall higher. Arising from this, molecular profiling techniques are being exploited by commercial multigene tests which accurately predict outcome and guide treatment in ER+ breast cancers. However, in Australia, these multi-gene tests are costly and not subsidised by Medicare. The prognostic power of current multigene tests derives from their accurate estimation of proliferation in the tumour. Therefore, we developed an alternative proliferation-based gene signature test, PROSPER, which can affordably estimate the risk of recurrence in ER+ breast cancer. To ensure future application to the clinical setting, PROSPER was measured in formalin-fixed paraffin-embedded tissue samples. Validation in the METABRIC breast cancer dataset revealed that PROSPER performed as well or better than the predictive signatures underpinning current commercial tests. In a prospective cohort of ER+ breast cancers, PROSPER was significantly correlated with clinical grade, proliferation marker Ki67 and with the results of a commercial multi-gene test. In a retrospective cohort, PROSPER was significantly correlated with Ki67, and disease-specific and overall survival. Optimization of the PROSPER signature to an easily applied test for application in the public pathology setting is underway. A successful outcome of this aim will result in considerable benefits to Australian patients and cost savings to the public health system.

Paper ID 130

Hydrogen peroxide in plasma-activated liquid and radiation-conditioned medium for cancer treatment

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Background: Cold atmospheric plasma-activated liquid (PAL) contains a variety of reactive oxygen and nitrogen species (RONS), which are generally short-lived and have potential to kill cells. Hydrogen peroxide has a relatively long half-life and is believed to be a key species of cell-killing in PAL. Due to the susceptibility of cancer cells to elevated RONS concentration, PAL is emerging as a promising cancer treatment and may be used in conjunction with radiotherapy.

Aim: Here, we seek to quantify the H_2O_2 concentration in PAL and in radiation-conditioned medium (RCM). We aim to first assess the dependence of H_2O_2 concentration in PAL on storage time and temperature and second to determine if the presence of cells influences the H_2O_2 concentration in PAL and RCM.

Methods: Amplex Red was used to detect H_2O_2 in fresh PAL, in one-week-old PAL stored at various temperatures and in fresh RCM alone and after 30 minutes incubation with DU145 prostate cancer cells. We determined the viability of these cells three days post treatment using the Alamar Blue assay.

Results: We identified H_2O_2 in both fresh PAL and RCM. One-week storage of PAL, at all storage temperatures, significantly reduced H_2O_2 concentration to the point where cell-killing effects were inhibited. Fresh PAL contained more H_2O_2 and killed DU145 cells more effectively than RCM. We found the H_2O_2 concentration was influenced by the presence of DU145 cells.

Conclusions: Our results demonstrate that PAL conveniently produces high levels of H_2O_2 which kills cells effectively. However, PAL should be made and used within hours to retain significant cell-killing properties.

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Paper ID 131

The novel role of GADD45a in regulating self-renewal activities in acute myeloid leukaemia

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Background: Acute myeloid leukaemia (AML) is a heterogenous and aggressive blood cancer common in children with no effective therapy against leukemic stem cells (LSCs) resulting in poor prognosis and high mortality with aberrant β-catenin signalling in a subset of AML. Low expression of growth arrest and DNA-damage inducible protein (GADD45a) is associated to poor clinical outcomes in AML but its role in LSCs and AML leukemogenesis is unknown.

Aim: This research aims to investigate GADD45a as a potential key regulator of the β-catenin signalling and its implication in LSC function and leukaemia progression.

Methods: Tumour burden was assessed using bioluminescence imaging in transgenic knockout of *Gadd45a* (*Gadd45a*$^{-/-}$) in murine LSCs and knockout of *GADD45a* in human AML cells by CRISPR/Cas9 *in vivo*. To further understand transcriptional regulatory mechanisms of *GADD45a*, single-cell RNA-seq was performed in AML patient-derived xenograft (PDX) cells and validated using RT-qPCR.

Results and Conclusions: Our studies discovered that *GADD45a* has a crucial role in AML LSCs. *Gadd45a*$^{-/-}$ leukemic cells developed a more aggressive leukemia with a shorter latency than *Gadd45a*$^{+/+}$ cells in mice, thus indicating *Gadd45a* loss in promoting leukemia development via an increase in aberrant self-renewal. In agreement with our findings in murine LSCs, deletion of *GADD45a* in human AML cells also showed increased tumour burden in immunodeficient mice. Furthermore, knockout of *GADD45a* increased β-catenin activity and critical self-renewal target genes in human AML cells. Our single-cell RNA-seq in AML PDX cells uncovered key *GADD45a* targets, such as *ferritin heavy chain* and *peroxiredoxin*. This study is the first to demonstrate the role of *GADD45a* loss in controlling LSC function and promoting leukemogenesis in AML murine and PDX models, thus showcasing *GADD45a* as a promising therapeutic target in AML. Low *GADD45a* can also serve as a potential biomarker to identify drug-resistant patient cohorts for LSC-targeted therapies.

Paper ID 132

Validation of an accurate automated multiplex immunofluorescence method for immunoprofiling melanoma

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Background: Multiplex immunofluorescence staining enables the simultaneous detection of multiple immune markers in a single tissue section, and is a useful tool for the identification of specific cell populations within the tumour microenvironment. However, this technology has rarely been validated against standard clinical immunohistology, which is a barrier for its integration into clinical practice.

Aim: This study sought to validate and investigate the reproducibility of a predictive multiplex immunofluorescence workflow, including tissue staining, imaging and analysis, in characterising the expression of immune and melanoma markers in both the tumour and its microenvironment.

Methods: Chromogenic immunohistochemistry (IHC), single-plex immunofluorescence and multiplex immunofluorescence were performed on serial tissue sections of a formalin-fixed paraffin-embedded (FFPE) tissue microarray containing metastatic melanoma specimens from 67 patients. The panel included the immune markers CD8, CD68, CD16, and PD-L1, and melanoma tumour marker, SOX10. Slides were stained with the Opal™ 7 colour Kit (PerkinElmer) on the Dako autostainer and imaged using the Vectra 3.0.5 microscope. Marker expression was quantified using Halo v.3.2.181 (Indica Labs).

Results and Conclusions: Comparison of the IHC and single-plex immunofluorescence revealed significant positive correlations between the percentages of CD8, CD68, CD16, PD-L1 and SOX10 markers (Spearman r = 0.965 to r = 0.657, $P < 0.0001$). Significant correlations were also observed for all of the markers following comparison between single-plex immunofluorescence and multiplex immunofluorescence staining (Spearman r > 0.9, $P < 0.0001$). Finally, correlation analysis of the three multiplex replicates revealed a high degree of reproducibility between slides (Spearman r > 0.9, $P < 0.0001$). Together, these data highlight the reliability and validity of this multiplex immunofluorescence workflow in accurately profiling the tumour microenvironment of FFPE metastatic melanoma specimens.

Translational significance: This validated multiplex panel can be utilised for research evaluating melanoma and its microenvironment, such as studies performed to predict patient response or resistance to immunotherapies.

Paper ID 133

Comparing patient monitoring and biofeedback methods for breast radiotherapy: the BRAVEHeart trial

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Background: Deep Inspiration Breath-Hold (DIBH) is used to reduce heart dose for left-sided breast cancer patients during radiotherapy. Where the heart is in close proximity to the treatment field, deep inspiration increases the distance from target to heart, reducing heart dose and lowering the risk of cardiovascular complications in later life. Surveillance of the chest wall position during treatment can verify that the breath-hold has been managed effectively, maintaining heart sparing.

Aim: The BRAVEHeart trial compares two visual-feedback systems for managing patient breath-hold, one measuring chest surface motion and the other abdominal motion. The trial hypothesis is that chest surface monitoring will more accurately reflect true chest wall displacement as the monitoring region is closer to and more rigidly linked with the chest wall.

Methods: Patients were randomised to use visual feedback from either the chest surface or abdominal monitoring system. The chest wall displacement during treatment relative to the planned position was obtained retrospectively by analysing beams-eye-view images captured during treatment.

System accuracy was quantified as the difference between the motion recorded in the external trace to the chest wall displacement measured with the in-treatment imaging. Reproducibility, the maximum difference between average amplitudes of DIBHs, and stability, the amplitude drift within a breath-hold, were assessed per treatment fraction.

Results: Analysis of the first 11 patients showed mean system accuracy in tracking the chest wall per breath-hold was 1.6 ± 1.6 mm and 1.6 ± 1.4 mm for chest surface and abdominal monitoring respectively. The chest surface monitoring system has improved reproducibility (0.6 ± 0.7 mm vs 2.7 ± 0.5 mm) and stability (0.1 ± 0.2 mm vs 0.2 ± 0.5 mm).

Conclusion: For the analysed treatments, the mean accuracy of both systems was equivalent, indicating that both chest surface and abdominal monitoring reflect true chest wall motion equally well. Breath-holds were more stable and reproducible for patients using the chest surface monitoring system.

Paper ID 134

Therapeutic targeting of KIT signalling in Acute Myeloid Leukaemia (AML)

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Background: Acute Myeloid Leukaemia (AML) is the most common and aggressive form of acute leukaemia, with a 5-year survival rate of just 24%. Over half of all AML patients harbour activating mutations in tyrosine kinases, such as the receptor tyrosine kinase KIT. KIT mutations are associated with poor clinical outcome, with lower remission rates in response to standard-of-care chemotherapy. Targeted, more effective therapies are required. KIT mutations lead to increased production of reactive oxygen species, which generates genotoxic DNA double strand breaks. The DNA-PK dependent DNA repair pathway, non-homologous end joining, is critical for the repair of DNA double strand breaks. This led us to investigate DNA-PK targeting as a therapeutic vulnerability in KIT mutant AML.

Aim: Evaluate DNA-PK activation and therapeutic targeting in KIT mutant cells.

Methods: The haematopoietic progenitor cell line FDC.P1 was transduced with an empty vector, wildtype KIT, or oncogenic KIT mutants (V560G, D816V). Drug toxicity was assessed by proliferation and annexin assays, and drug synergy was evaluated using Chou-Talalay and Webb analyses. Signalling pathways were profiled using mass-spectrometry based phosphoproteomics.

Results and Conclusions: Targeted quantitative phosphoproteomic profiling identified phosphorylation of DNA-PK at threonine 2599 in KIT mutant cells, indicative of DNA-PK activation. Accordingly, proliferation assays revealed that KIT mutant FDC.P1 cells were more sensitive to DNA-PK inhibitors (NU7441, M3814) than wildtype KIT cells expanded in GM-CSF, or empty vector controls. Inhibition of KIT signalling (Dasatinib, Ibrutinib) combined with DNA-PK inhibition led to synergistic cell death. Discovery phosphoproteomics revealed that the combination of Dasatinib and M3814 treatment inhibited MTOR, MAPK, and PI3K signalling in D816V mutant cells, with synergistic inhibition of Myc phosphorylation. This study provides insight into the oncogenic pathways regulated by DNA-PK beyond its canonical role in DNA repair, and demonstrates that DNA-PK is a promising novel therapeutic target for this poor-prognosis AML subtype.

Paper ID 136

Is Prognosis Worse for People with Multiple Versus Single Primary Melanoma?

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Background: Patients with a primary melanoma may develop more than one in their lifetime. It is unclear whether mortality is worse after diagnosis of multiple primary melanoma (MPM) compared with single primary melanoma (SPM).

Aim: We compare overall and disease-specific mortality for SPM versus MPM at pre-specified landmark timepoints, in a population-based Australian sample.

Methods: We analysed data from a population-based cohort of 3,869 patients diagnosed with primary in situ or invasive cutaneous melanoma in New South Wales, Australia in 2006-07 and followed up until 2018 (median 11.9 years) using linked mortality and cancer registry data. We compared overall mortality and melanoma-specific mortality for patients who developed a single versus multiple primary melanomas, adjusting for other clinico-pathological prognostic indicators, using Cox proportional hazard models. The primary analysis was based on pathological features from the thickest tumour for MPM patients, however sensitivity analyses were performed using the first and last primary melanoma.

Results: The cohort consisted of 3,869 patients (2,929 SPM and 940 MPM) and 5,504 melanoma lesions (including 2,575 lesions from MPM patients). The primary multivariable analysis showed MPM was associated with lower mortality from all causes and melanoma compared with SPM with a hazard ratio of 0.62 (95% CI: 0.54-0.71, $p<0.001$) and 0.37 (95% CI: 0.32-0.43, $p<0.001$) respectively. These findings were also supported by the sensitivity analyses.

Conclusions: The diagnosis of MPM does not worsen mortality compared to a SPM, in fact it was associated with improved survival. This finding might be related to skin examination behaviours, biological or clinical factors.

Paper ID 137

Acceptability and feasibility of lung cancer screening in Australia

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Background: Lung cancer is the number one cause of cancer death worldwide. International trials have demonstrated that targeted screening using low dose computed tomography (LDCT) is effective in significantly reducing lung cancer mortality and detecting cancers at an early stage. Implementation of screening in the high-risk population presents complex challenges that need to be clearly understood prior to policy change.

Aim: To elicit stakeholders' (health care providers, policymakers) views about barriers and enablers to implementation of lung cancer screening in the Australian setting.

Methods: We conducted 18 focus groups in 2021, either face-to-face or using the Zoom platform, with 62 health professionals, researchers and managers and policy makers in current screening programs. Focus groups included a structured presentation about lung cancer and screening. Participants took part in facilitated discussions for about one hour. The focus group content was analysed thematically.

Results: The large majority of participants considered lung cancer screening to be feasible and acceptable but identified a wide range of challenges to implementation. Challenges included participant factors such as encouraging participation from priority groups (those at high-risk), whilst ensuring that access and equity issues were carefully considered in designing a screening program. Health system factors included workforce resources, physical infrastructure (e.g. access to CT scanners) and establishing a quality assurance program. Participants strongly advocated for developing awareness and education campaigns that engaged participants and health professionals, as well as streamlined referral processes for initial entry and follow-up scans. Practical considerations, such as using mobile vans, were also emphasised.

Conclusions: Key stakeholders readily identified the complex challenges that need to be addressed to ensure lung cancer screening is acceptable and feasible in Australia. These findings regarding feasibility are highly relevant to the early scoping of a potential national lung cancer screening program announced by the Australian Government in May 2021.

Paper ID 138

Patient Reported Measures – feasibility of collecting for Arabic speaking patients

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Background: Patient Reported Measures (PRMs) present a powerful catalyst for value-based health care systems. They enable a patient-centred approach, whereby patients can give direct and timely feedback, improving outcomes, experience and quality of care.

Aim: This pilot project aimed to determine the feasibility of collecting PRMs from Arabic speaking cancer patients with low or no English proficiency for use by clinicians using the paper-based Edmonton Symptom Assessment Scale (ESAS-r) questionnaire.

Method: A bi-lingual Project Officer was employed part-time to administer the ESAR-r questionnaire to Arabic speaking patients attending a metropolitan Cancer Centre outpatient clinic, prior to their appointments with clinicians, over a 5-month period. An evaluation was conducted to assess project implementation, cultural appropriateness of the questionnaire and early outcomes produced as a result of the pilot project. Data was collected daily on completion rates and appropriateness of the tool. Interviews with key stakeholders (n=4) were also conducted.

Results: The pilot was largely implemented as intended and successfully established, for the first time in New South Wales, a process to collect PRMs using a paper based in-language tool. Forty-eight (48) cancer patients of Arabic speaking background completed the questionnaire, which was found to be culturally appropriate. Out of the 48 patients, 28 patients (58.3%) required little explanation to understand the surveys purpose. Of those that needed assistance to complete the survey (41/48), 78% received help in Arabic, 20% in both English and Arabic, and 2% in English. Qualitative data suggested the tools usefulness in improving symptom reporting, patient-health professional communication and the identification of unmet needs.

Conclusion: The pilot evaluation demonstrated the feasibility of collecting PRMs from Arabic speaking cancer patients with low or no English proficiency and provided early evidence on the usefulness of collecting in-language PRMs. Results can be used to inform future PRMs work for patients of culturally and linguistically diverse backgrounds.

Paper ID 139

Caregiver Fear of Cancer Recurrence: A Qualitative Meta-synthesis

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Background: Fear of cancer recurrence (FCR) is a common and distressing issue for cancer survivors. Recent studies suggest informal caregivers also report significant concerns about possible recurrence of the survivor's cancer. It is not clear whether caregivers have unique FCR experiences that differ from those identified by survivors.

Aim: The aim of this systematic review was to synthesise qualitative research examining caregiver experiences of FCR.

Methods: CINAHL, Embase, PsychINFO and PubMed electronic databases were searched to identify qualitative studies reporting on caregiver FCR. Studies of adult caregivers providing care for adult cancer patients published to July 2020 were included (Prospero registration CRD42020201879).

Results: Of the 12 studies included, none identified FCR as a primary focus, but reported FCR as an emerging theme. Thematic analysis identified three themes, two of which (uncertainty and fear of the future), and their subthemes (triggers, and hypervigilance) align with patient experiences. A third theme, caregiver's role as the protector was unique to the caregiver experience. An overarching theme, fear of losing a loved one explained the relationship between the identified themes.

Conclusions: There is relatively little research examining FCR in caregivers. While caregivers describe similar themes to those reported by survivors, the protective role caregivers adopt to shield the survivor from cancer-related stimuli has not been previously highlighted. Our results suggest this identified need to protect the survivor from both external factors relating to cancer as well as their own personal concerns has implications for communication within the dyad. It is currently unclear how well caregiver experiences of FCR align with already defined survivor FCR models. Further research is needed to obtain a better understanding of how caregivers' and survivors' experiences of FCR differ, to inform the development of interventions which specifically target the needs of caregivers.

Paper ID 140

Can MRI be used for mid-treatment adaptation of radiation therapy for prostate cancer?

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Background: A personalised approach to radiation therapy (RT) of prostate cancer (CaP) requires accurate spatial mapping of tumour biology. Quantitative MRI (qMRI) can map biological properties in tissues. In principle, mapping changes in qMRI values during treatment provides an opportunity to identify radioresistant sub-volumes, enabling adaptive treatment strategies to minimise risk of local recurrence.

Aim: We report early findings of a prospective study designed to identify imaging features as potential candidate biomarkers for radioresistant disease.

Methods: Magnetic resonance imaging in ten CaP patients was performed at 2 time points prior to treatment to test spatial and temporal stability of imaging features, and 2 time points during treatment. MRI sequences included T2w, diffusion weighted imaging (DWI) and blood oxygen level dependent (BOLD) imaging. Apparent diffusion coefficient (ADC), T1 and R2* parametric maps were derived from the imaging studies. Patient datasets were co-registered and corresponding regions of interest (ROI) were generated within benign and tumour volumes for analysis.

Results: Pre-treatment test, retest data indicated a mean coefficient of variability in tumour ADC, T1 and R2* were 8.9%, 2.7% and 10.9%, respectively and provide a threshold for identifying significant changes in these parameters during treatment. A decrease in tumour size and changes in spatial distribution of qMRI parameters within the lesions were visually apparent. Based on a standard image processing workflow, difference between average qMRI parameters pre- and during treatment were not significant. These results indicate that acute changes such as oedema and changes in tumour activity require more complex analysis methods, such as radiomics to differentiate radio-responsive and radio-resistant disease.

Conclusions: Analysis of longitudinal qMRI data is challenging due to changes in tissue structure following irradiation. A radiomics-based approach is required to conclusively evaluate the use of qMRI parameters in RT response assessment.

Paper ID 141

Cancer patients post hospital discharge - how/when should therapists intervene: A Systematic review

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Introduction: Advances in cancer treatment over the last decade have led to increased survival rates. As a result, survivors are living longer with and beyond cancer, often with greater levels of morbidity. Occupational therapists, with their focus on improving function and participation, are well suited to assess and intervene. Despite this, little research exists to demonstrate the efficacy of interventions and value of the occupational therapy role. This systematic review aimed to review how and when occupational therapists deliver services for adult patients with cancer and identify where they add the most value in order to provide an evidence base for clinicians in the field.

Methods: A systematic search was conducted of six electronic databases. Eligible studies reported on occupational therapy interventions targeting management of cancer symptoms, rehabilitation or environmental modifications for adult cancer patients discharged from acute hospital services. Data extraction and quality assessment were undertaken by two reviewers, and narrative synthesis summarised the attributes and treatment outcomes of each intervention.

Results: Nine articles were included from a total of 309 articles retrieved. Eight different interventions were reported for people with cancer (n= 531). Small sample sizes and methodological quality precluded any formal analysis however; intervention components that showed positive results were person-centred, individualised, and included regular monitoring and flexibility in care, with input from multi-disciplinary health professionals.

Conclusion: Despite inconclusive support of any particular type of intervention, the review did provide support for the following intervention components, and future research in these areas is required: person-centred, individualised treatment that supports fluctuating patient needs; inclusion of monitoring and flexibility in care; adequate treatment duration and intensity to elicit change; optimal timing of treatment; selection of sensitive outcome measures that specifically match intervention components; and use of multi-disciplinary health professionals as part of intervention delivery. The review has important translational implications by providing guidance for therapists designing rehabilitation programs to improve the lives of people with cancer.

Paper ID 142

Psychosocial outcomes and QoL in advanced colorectal cancer survivors: A qualitative exploration

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Background: Approximately 18% of colorectal cancer (CRC) diagnoses are advanced cancer, while 30-40% of patients develop recurrence after treatment with curative intent. More modern treatments enable longer survival for people with advanced CRC, including: cytoreductive surgery and hypothermic intraperitoneal chemotherapy (CRS-HIPEC), pelvic exenteration, liver resection, and palliative chemotherapy without surgery. Yet, virtually no qualitative research has compared the perspectives and quality of life (QoL) experiences of survivors of these different treatments. This study aims to fill this gap.

Methods: Approximately N=40 adult survivors of CRC are being recruited from two major Australian hospitals 0.5-2 years post-treatment or post-diagnosis. All participants will complete the Functional Assessment of Cancer Therapy – Colorectal (FACT-C), Distress Thermometer, and Comprehensive Score for Financial Toxicity (COST) questionnaires. Questionnaire data, participant demographics, and clinical data will undergo descriptive analysis to characterise the sample. Participants will participate in a qualitative semi-structured telephone interview, analysed via the framework approach of thematic analysis. Qualitative interviews explore QoL, survivorship experiences, employment and finances, supportive care needs, stigma and social functioning, and impacts of COVID-19.

Results: Preliminary analysis of 30 interviews (n=10 CRS-HIPEC, n=9 pelvic exenteration, n=5 liver resection, n=6 palliative chemotherapy) reveals some advanced CRC survivors report post-surgical complications and chemotherapy-induced peripheral neuropathy, which can limit physical activity and daily functioning. Participants reportedly manage these through distraction, positive reframing, and contacting other CRC survivors. Most participants appeared satisfied with their cancer treatment teams. Some viewed their GPs as important coordinators in their health care. Some CRC survivors viewed the change to telehealth due to COVID-19 as less personal; however, rural/regional participants prefer its convenience.

Conclusions: The study findings will help guide development of interventions to improve the survivorship experience of patients who receive treatment for advanced CRC. This may include an information booklet, patient-reported outcome measure, clinical pathway, or targeted intervention.

Paper ID 143

Gas plasma activated liquid inhibits cancer: a new take on radiation therapy

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Radiotherapy produces Reactive Oxygen and Nitrogen Species (RONS) in the body that cause cell death. We have developed a novel physical plasma device to load RONS into a liquid, producing plasma activated liquid (PAL) for treating cancer. The aim of this study is to determine the cytotoxicity of PAL relative to radiation therapy and their combined use to identify potential synergies.

Method: A clonogenic assay was used to compare the responses of cells to PAL and radiotherapy (6MV photons) and in combination. PAL was created using a physical plasma directed onto Hartmann's solution and transferred to DU145 prostate cancer cells in 6-well plates for a range of dilutions. The PAL was then replaced with growth medium after 30 minutes incubation and the plates returned to the incubator to perform the clonogenic assay on day 7 after treatment.

Results: For both PAL and radiation treatment, cell survival was found to decrease as a function of dose. The survival following treatment with PAL followed by radiation was less than the survival fraction expected, determined by multiplying the survival fractions to the individual treatments.

Conclusion: PAL treatment followed by radiation treatment yielded a synergistic response suggesting an opportunity to use PAL increase cytotoxicity without additional ionising radiation dose.

Paper ID 144

In Radiation Therapy, are all 3Gy fractions equal?

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Background: Although radiotherapy treatments are delivered in prescribed fractions, the delivery schedule within a fraction is not normally considered to be important. The aim of this study is to determine if it makes a difference when the treatment fraction is delivered in two equal parts with a short time interval between them.

Method: Two prostate cancer cell lines (LNCaP hormone sensitive, DU145 hormone insensitive) and a normal prostate (PNT1A) cell line were exposed to a 6MV photon beam, to a grid field with a period of 5 mm, or to a uniform field of the same mean dose. A clonogenic assay was performed to quantify survival. The dose was delivered in two equal parts separated by a range of time intervals, *t* from 0 to 120 minutes. The therapeutic ratio was calculated as the survival of normal cells relative to that of cancer cells.

Results: For the LNCaP cell line, a significant therapeutic benefit was found in delaying the second dose by more than 10 minutes (uniform field) or 30 minutes (grid field). For the DU145 cells, there was no therapeutic benefit in splitting the dose for either uniform or grid fields.

Conclusion: The results show that for a subgroup of cancers, all 3Gy fractions are not equal. There appears to be an untapped opportunity in intra-fractional modulation in both space and time.

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Paper ID 145

Cyclin E1 (*CCNE1*) gene amplification assessment in prospectively recruited ovarian cancer patients

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Background: High cyclin E1 (*CCNE1*) gene copy number has been associated with resistance to primary chemotherapy and poor outcome in women with high-grade serous ovarian cancer (HGSC). Targeted agents that may be effective against *CCNE1*-amplified tumours are in development and entering early-phase clinical trials. There is therefore a need for reliable methods to determine *CCNE1* copy number variation (CNV) in clinical samples.

Aim: Assessment of somatic *CCNE1* CNV by droplet digital PCR (ddPCR) and Single Nucleotide Polymorphism (SNP) microarray in the INOVATe (Individualised Ovarian Cancer Treatment through Integration of Genomic Pathology into Multidisciplinary Care) cohort.

Methods: *CCNE1* CNV was evaluated by ddPCR (Bio-Rad) in 497 ovarian cancer cases (n=333 HGSC, n=164 non-HGSC). In 129 HGSC and 22 non-HGSC cases, SNP array (Illumina) data was available as an independent method for validation. SNP array was analysed by two methods: Genomic Identification of Significant Targets in Cancer (GISTIC) and Genome Alteration Print (GAP). The effect of tumour cell content, *TP53* variant allele frequency and ploidy were investigated.

Results: Overall, *CCNE1* amplification/gain was identified by ddPCR in 16% (54/333) of HGSC, and 5% (8/164) of non-HGSC cases. Gene amplification of *CCNE1 (*≥8 copies, ddPCR) was validated by SNP array in 100% of the cases, and high concordance was also observed for cases with normal *CCNE1* (~89%), however assessment of *CCNE1* gain (≥4-<8 copies, ddPCR) was less concordant between the methods (50%). Tumour cell content was not a major contributing factor in the discordant cases (*TP53* variant allele frequency average of 77%), however ploidy may be a confounder, with most discordant tumours found to be tetraploid (83%). Spearman's correlation coefficient between ddPCR and GISTIC was 0.67 (95%CI 0.52-0.79). *CCNE1* amplification was exclusive of *BRCA1/2* mutations, as previously reported.

Conclusions: *CCNE1* copy number variation in the INOVATe cohort is consistent with previous studies. While additional validation will be required for assessment of *CCNE1* low-level copy number gain, our results suggest that ddPCR may provide an accurate, rapid, and low-cost screening test for *CCNE1* gene amplification.

Paper ID 147

How Cancer Health Care Professionals Assess & Manage Anxiety in Patients: Clinical Vignettes

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Objectives/Purpose: People with cancer face many emotional, psychological and practical day-to-day demands on top of the debilitating physical impacts of the disease and its treatment. The importance of addressing patient anxiety is widely acknowledged by National Cancer Control bodies and cancer health care professional organisations. However, the degree to which cancer healthcare providers (CHCPs), , engage in the provision of psychosocial care is unknown. The aim of this study was to explore CHCP confidence and clinical management practices in dealing with anxiety in their patients.

Methods: Australian CHCPs were invited to complete an online self-administered questionnaire. As part of the survey six patient vignettes were presented, depicting cancer patients with varying levels of anxiety, stages and types of cancer, and various underlying concerns. Participants were asked about their approaches to treatment.

Results: Responses varied markedly between vignettes, indicating that clinicians tailored their responses to the presentation portrayed. Participants were less willing to provide treatment themselves when they perceived the patient's anxiety to meet the threshold for a disorder. Recommendations for pharmacological management were common, especially for benzodiazepines. Non-pharmacological strategies were recommended in every case.

Conclusion and Clinical Implications: CHCPs tailor their approach to the individual, and overall are likely to recommend a mix of pharmacological and non-pharmacological approaches. The frequency of recommendations for benzodiazepine use (in contrast to SSRIs in accordance with most guidelines for the treatment of anxiety), suggests a role for professional education for the management of anxiety in a cancer context.

Paper ID 148

Phosphoproteomics predicts novel treatment targets for FLT3-ITD+ AML resistant to targeted therapy

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Background: Acute myeloid leukaemia (AML) is driven by the malignant transformation of haematopoietic stem/progenitor cells. *FLT3* represent the most recurrent driver mutation in AML, associated with resistance to standard-of-care chemotherapy in up to 80% of patients. The two most common mutations in FLT3 correspond to internal tandem duplications (FLT3-ITD) and missense point mutations (FLT3-TKD) that maintain the constitutive activation of oncogenic pathways. The commonality of these mutations highlights FLT3 as a therapeutic target and tyrosine kinase inhibitors (TKI) were recently approved for the treatment of FLT3-ITD+ patients. However, acquisition of additional TKD mutations (FLT3-ITD/TKD) drives secondary resistance to this new treatment strategy. Oncogenic signalling activated in response to this resistance-causing mutation is yet to be determined.

Aims: To perform phosphoproteomic profiling of FLT3 mutant AML at relapse to discover novel and more effective therapeutic targets for patients with advanced disease.

Methods: Unbiased and targeted quantitative phosphoproteomic profiling using isogenic myeloid progenitor cells harbouring human FLT3-wild type (FLT3-WT), FLT3-ITD (diagnosis), FLT3-TKD (D835V and D835Y - diagnosis), and the double mutant FLT3-ITD/TKD (FLT3-ITD/D835V and FLT3-ITD/D835Y - relapse) was performed in biological triplicates (n=30). Tandem-mass tagging (TMT-10plex) nLC-MS/MS, Parallel Reaction Monitoring (PRM), and Field Asymmetric Ion Mobility Spectrometry (FAIMS) using TiO2-enriched phosphopeptides was performed. Analysis using Proteome Discoverer, Skyline, Perseus, and Ingenuity Pathway Analysis (IPA) uncovered signalling changes and downstream therapeutic targets.

Results: Significantly decreased expression (-1.38+/-0.20, $p<0.01$) of FLT3 protein was seen in cells harbouring FLT3-ITD/TKD mutations compared to controls. Kinase set enrichment analysis of phosphoproteomic data predicted significant activation of PRKCA ($p<0.01$), AURKB ($p<0.01$), NEK2 ($p<0.05$), RAF1 ($p<0.05$), kinases related to MAPK signalling ($p<0.05$), and inactivation of FLT3 ($p<0.001$), and CDK2 ($p<0.01$) in FLT3-ITD/TKD when compared to FLT3-ITD. IPA further revealed significantly increased DNA repair pathways. Simultaneous targeting of DNA repair in combination with PKC inhibition was highly synergistic (CI=0.6) highlighting clinically relevant treatment approaches for relapsed AML patients.

Conclusions: Activation DNA damage and repair pathways in response to resistance-causing mutations is a potential therapeutic opportunity in patients harbouring resistance-causing mutations.

Paper ID 149

Feasibility of micro-learning for cancer patient health education

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Background: Individuals undergoing cancer treatment often receive a large amount of information about their condition very quickly after diagnosis. It can be challenging for patients to retain key information about managing their condition, or side-effects of their treatment as a result. Digital technologies can provide an invaluable mechanism for disseminating education to patients about their cancer treatment. Online micro-learning is a digital technology that may be particularly well suited for disseminating education to cancer patients, as it is a way of disseminating key information in small bundles in a manner potentially quick and easy for patients to engage with.

Aim: To evaluate the feasibility of using an online micro-learning platform to delivery information on side-effects of chemotherapy to patients with advanced lung cancer.

Methods: A mixed methodology is being used for this study. Quantitative data includes metrics from the micro-learning platform on participant progress and program completion. Qualitative data includes a post-program online survey and semi-structured interviews.

Results: A total of 22 lung cancer patients have been enrolled in the micro-learning platform. Of this cohort 14 have completed the program, and an additional 5 have partially completed it. Ten participants have completed a post-program survey and four have participated in a semi-structured interview. Preliminary analysis of qualitative data indicates that the content of the micro-learning program aligns with the experiences of patients undergoing chemotherapy. Participants have found the program a positive experience that augments existing mechanisms for receiving information on side-effects of their cancer treatment.

Conclusions: Micro-learning has potential to be an accessible tool for improving patient self-efficacy managing side effects of chemotherapy. The translational significance of this work includes increasing understanding of the barriers and enablers to supporting patients in using micro-learning to increase knowledge around the identification and management of chemotherapy side-effects.

Paper ID 150

Predictive immune signatures for cancer immunotherapy – from bench to bedside

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Background: The success of checkpoint therapy has highlighted the involvement of the immune system in cancer control. However many questions remain unanswered, both in terms of understanding how checkpoint therapy works, and how we can best use it in clinical practice. Therapies that target the PD-1/PD-L1 pathway can generate major clinical benefit, but usually in only a minority of patients. Finding ways to predict which patients will respond, and how to convert non-responder patients to responders, are still crucial unmet needs.

Aim: To use highly multiparametric immune analysis to further our understanding of checkpoint therapy targeting the PD-1/PD-L1 pathway.

Methods: We used mass cytometry antibody panels of up to 40 markers to analyse cryopreserved peripheral blood mononuclear cells from cancer patients (advanced melanoma and NSCLC) who were about to start anti-PD-1/PD-L1 therapy. Manual gating was used to identify over 150 distinct cell populations in each patient. Clinical response (RECIST) at 3 months was then used to classify patients into responder and non-responder groups, followed by machine learning to identify the combination of cell subsets (the immune signature) that best distinguished the two groups.

Results: Our analysis revealed an immune signature that predicted non-responder status in both melanoma and NSCLC with unprecedented precision. Within the signature, the size of multiple T and NK cell subsets, including many that would not directly contact the cancer, was reduced in non-responder patients, consistent with a systemic effect of the immune response to the cancer or the cancer itself. We are currently working to identify the systemic factors responsible for non-responder status, with the aim of restoring immune reactivity before initiation of checkpoint therapy. We are also adapting signature analysis to a tube-based fluorescence cytometry assay for rapid patient screening.

Conclusions: Our immune signature test will allow PD-1/PD-L1 checkpoint therapy to be administered to those patients who will benefit the most. It has also provided a unique insight into why the majority of patients do not respond, and generated new approaches to reversing non-responder status.

Paper ID 151

Radiomics: defining mammographic image characteristics to enable a more reliable gist signal?

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Abnormal lesions in mammograms can be detected by a radiologist in a momentary glimpse of an image. This immediate understanding of the image is called the gist response, however little is known regarding the image features that make this possible. The current work analyses the effect of mammographic characteristics of the lesion and lesion's immediate background as well as the global image characteristic on gist response. These features using the latest radiomic approaches are extracted from mammograms to find the optimum dataset that can be utilised in developing a model as a means to predicting the presence of an abnormal lesion in the breast tissue. The work is required, since the gist as we know it, is a noisy signal with some radiologists exhibiting strong and others weak gist abilities. Once we understand more about the image parameters on which gist response relies, we can develop a breast cancer detection model using more objective measures and machine learning approaches. This project aims to develop such a model with acceptable capabilities of interpolation and extrapolation (i.e. generalisable model). We call this model the Automated Breast Cancer Detection model (ABCD) which should help the early detection of breast cancer and reduce mortality rates. Our work to date and early results on key image characteristics will be presented.

Paper ID 152

Melanoma surveillance on their own device: can patients identify subsequent melanoma?

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Background: Patients may lead their own surveillance for subsequent new primary or recurrent melanoma, but the comparative safety, feasibility and acceptability is unknown.

Aim: To investigate whether patient-led surveillance of subsequent melanoma is safe, feasible and acceptable.

Methods: 100 patients previously treated for localised melanoma were recruited from specialist and primary care clinics in New South Wales, Australia. Participants were randomised (1:1) to six months of patient-led surveillance (intervention: usual care plus reminders to perform skin self-examination (SSE), patient-performed dermoscopy, teledermatologist assessment, and fast-tracked unscheduled clinic visits) or clinician-led surveillance (control: usual care). The primary outcome was the proportion of patients approached to participate who were randomised. Secondary outcomes included patient-reported outcomes (SSE knowledge, attitudes and practice, psychological outcomes, other healthcare use) and clinical outcomes (clinic visits, skin surgeries, subsequent new primary or recurrent melanoma).

Results: Between November 2018 and May 2019, 481 patients were approached to participate, of whom 116 were ineligible and 100 (21%; 95%CI:17% to 25%) were randomised to patient-led surveillance (n=49) or clinician-led surveillance (n=51). Data were available on patient-reported outcomes for 66 participants, and on clinical outcomes for 100 participants. Compared with clinician-led surveillance, patient-led surveillance increased SSE frequency and thoroughness, had no detectable effect on psychological outcomes, and increased clinic visits, skin lesion excisions, and subsequent melanoma diagnoses. New primary melanomas were diagnosed in 8 intervention group participants (16%) and in 3 control group participants (6%). All 5 detected at unscheduled visits were in the intervention group (between-group difference: 10%; 95%CI: 2% to 19%). No recurrences were diagnosed.

Conclusion: Patient-led surveillance following treatment of localised melanoma appears safe, feasible and acceptable. A larger trial of the same intervention will generate evidence on comparative effects on

health, psychological and resource use outcomes and assess whether patient-led surveillance may be translated into policy and practice.

Paper ID 154

Implementation of VIETRAD in Vietnam significantly improves detection of breast cancer

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Background: Breast cancer is the most common cancer in Vietnamese women with over 10,000 new cases annually and over 80% of patients with late stage disease. Early cancer detection depends on accurate interpretation of breast images by radiologists; and previous data from our BREAST group showed that Vietnamese radiologists displayed low diagnostic efficacy when reading mammograms. In 2020, the VIETRAD program, a partnership between the University of Sydney and the Health Strategy and Policy Institute of Vietnam funded by the Aus4Innovation (DFAT), was launched with two workshops conducted in Hanoi and Ho Chi Minh City.

Aims: To evaluate the performances of Vietnamese radiologists in reading mammograms over the three training sessions.

Methods: 64 radiologists were asked to read and find the cancer location on 60 Vietnamese mammograms (the first session), 60 Australian mammograms (the second session) and 80 mammograms of both Australian and Vietnamese women (the third session). After each session, radiologists reviewed the answers with Australian BreastScreen experts. Radiologists' performances were calculated in specificity, sensitivity, lesion sensitivity, ROC and JAFROC and compared among three reading sessions.

Results: The radiologists increased 9.3% in sensitivity, 6.7% in lesion sensitivity, and 10.6% in JAFROC in the third session compared with the second reading session. The specificity of radiologists in the third session was 19.5% higher than the first session. Radiologists had 19.1% of increase in specificity when reading the Vietnamese mammograms in the third session compared with the first session and a 13.8% increase with Australian mammograms in the third session compared with the second session.

Conclusions: The performance of Vietnamese radiologists improved through the VIETRAD workshops. Further improvement and engagement from radiologists when VIETRAD is implemented in hospitals in the north, the south and the central regions of Vietnam are expected.

Paper ID 155

Development of nanoparticles as biosensors for diagnosis of mucosa changes insitu during colonoscopy

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Background: Detection of mucosal abnormalities in the bowel using colonoscopy relies on visual interpretation and colonoscopist experience. Quality assurance metrics propose a minimum standard for adenoma detection rate (ADR) at 15% with an aspirational ADR of 20%. Often difficult to recognise polyps are missed (e.g. non-elevated serrated adenoma) even in the hands of experienced colonoscopists. Therefore, we identify a need to develop suitable classes of surface biosensors which show differentiated affinity of colorectal mucosa with and without polypoid changes.

Aim: The aim of this study is to test suitable class(es) of nanoparticles as surface biomarkers for in situ recognition of colorectal mucosa changes at colonoscopy.

Methods: Animal model with intestinal disease was introduced chemically by using the azoxymethane/dextran sodium sulfate (AOM/DSS) mouse model. At the end point, the fresh intestinal tissues were collected and treated with nanoparticles in cold PBS. The tissues were washed and fixed in 4% formalin for 24 hours, followed by 80% ethanol. The fixed tissue was rolled to a Swiss roll, embedded in wax, and sectioned for H & E histology and Prussian blue (iron staining).

The treated intestine and Swiss role samples were imaged on the IVIS fluorescence animal imager. The H & E and Prussian blue slides were imaged on a slide scanner.

Results and Conclusions: The inflammatory intestinal mucosa from the animal model were assessed from the H & E sections. The fluorescent and Prussian blue images showed different binding of nanoparticles to mucosa and submucosa layers of intestinal tissues. The particles were also observed inside the area with high concentration of immune cells such as in Peyer's patches.

This study will potentially provide a new identification method to assess colon adenoma in situ during colonoscopy. If the in vivo study is proven successful, this study can be translated to clinical practice.

Paper ID 156

Dynamics of radiation-induced remodelling in 3D spheroids of head and neck squamous cell carcinoma

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Background: The dynamic molecular and cellular nature of tumour cell remodelling after exposure to ionising radiation is an acknowledged but yet under-investigated phenomenon. These changes at the cellular and molecular levels, play key roles in tumour invasion, metastasis and resistance to therapy, all of which are strong indicators for poor prognosis and survival.

Methods: In this study, we have used 3D tumour spheroids from human oral squamous carcinoma cells and patient-derived tumour samples combined with next-generation RNA sequencing and comparative analysis to tumour data bases to highlight key cellular and molecular dynamics in response to ionising radiation.

Results: Our study demonstrates a key radiation-induced phenotype switch along the epithelial-mesenchymal axis that plays functional roles in tumour cell invasion and resistance to radiation. Further, molecular analysis highlighted Wnt signalling pathway among others as a key driver for this phenotype switch, inhibition of which resulted in heightened response to radiation and significant loss of tumour cell invasion. Our study further highlights important epigenetic and immune modulators broadening the image for the pathways involved in post-radiation remodelling in 3D tumour cell spheroids.

Conclusion: The current study highlights key cellular and molecular dynamics in response to radiation, knowledge of which will result in improved treatment strategies mitigating the adverse outcomes commonly observed downstream of radiation.

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Engineering p53 wild-type, knockout and gain-of-function mutant ovarian cancer panels with CRISPR

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Background: *TP53* is mutated in almost 100% of high-grade serous ovarian cancers. We have employed CRISPR-Cas9 tools to generate isogenic p53 ovarian cancer cell lines for the purpose of discovering new opportunities for therapeutic targeting of mutant p53 and to reveal biological associations.

Aim: To use CRISPR-Cas9 gene editing to create isogenic ovarian cancer cell line panels differing at the p53 locus (wild-type, knockout and gain-of-function (GOF) mutation). Further, to characterise these panels for factors including spheroid formation, response to DNA damage-based chemotherapeutics and molecular target drugs.

Methods: One wild-type p53 cell line (A2780) and two p53 mutant cells line (OV207, p.R273H; TYK-nu, p.R175H) were the focus of this study. *TP53* single guide RNA (sgRNA) was cloned into the pSpCas9(BB)-2A-GFP (PX458) plasmid vector (#48138, Addgene) that contains sequences that express a human codon-optimised *S.pyogenes* Cas9 (hSpCas9) nuclease and Green Fluorescent Protein (GFP). This construct was transfected into cell lines and single GFP positive cells sorted using the BD FACSMelody cell sorter. We used the cytosine base editor plasmid pCMV_AncBE4max_P2A_GFP (Addgene #112100) modified to contain sgRNA sequences from the PX458 plasmid. Screening for p53 was undertaken using In-Cell Western followed by Sanger sequencing. Cell lines were challenged with cisplatin and the mutant p53 target drug APR-246.

Results: We generated a p53 knockout and engineered the p.M246I *TP53* mutation into A2780 cells. GOF mutant cells displayed increased resistance to cisplatin compared with wild-type and, as expected, were unable to activate the p53 target gene *CDKN1A*. Work is on-going to revert mutant *TP53* to wild-type in OV207 and TYK-nu and conduct functional studies.

Conclusions: We have engineered an isogenic cell line panel in A2780 cells and demonstrated differential functional effects. Isogenic panels generated using CRISPR-Cas9 are powerful tools for the study of cancer genes, including the potential to be used for drug discovery.