Tuesday 8 August
L’Aqua - Dockside Darling Harbour
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#scitcrs2017
Who We Are

Sydney Catalyst is the translational cancer research centre of central Sydney and regional NSW. We're driven by an outstanding team of researchers, clinicians and students drawn from our diverse range of member groups and institutions.

With more than 600 individual members working across the translational research pipeline, we have the unique ability to facilitate rapid translation of scientific discoveries into clinical policy and practice to improve outcomes for people affected by cancer.
WHO IS SYDNEY CATALYST?

Our Governing Council (GC)

**Professor John Simes**  
Director, Sydney Catalyst  
Senior Principal Research Fellow and Director, NHMRC Clinical Trials Centre  
Professor of Clinical Epidemiology, NHMRC Clinical Trials Centre, Sydney Medical School, University of Sydney  
Medical Oncologist, Chris O’Brien Lifehouse/Royal Prince Alfred Hospital, Sydney  
Co-Founding Director, Australian Clinical Trials Alliance  
Fellow of the Australian Academy of Health and Medical Sciences  
Board member, Australasian Gastro-Intestinal Trials Group Incorporated

**Professor Philip Hogg**  
Chair in Translational Cancer Research for Sydney Catalyst and NH&MRC Clinical Trials Centre  
Head, ACRF–Centenary Cancer Research Centre  
Co Chair Sydney Catalyst Pilot and Seed Committee

**Professor Michael Boyer**  
Chief Clinical Officer and Conjoint Chair of Medical Oncology (Thoracic Oncology), Chris O’Brien Lifehouse and Sydney Catalyst GC Chair

**Professor Phyllis Butow**  
NHMRC Senior Principal Research Fellow,  
Chair, Scientific Advisory group, Sydney Catalyst  
Founding Director of Centre for Medical Psychology and Evidence-based Decision-making (CeMPED)  
and the Psycho0-Oncology Cooperative Research Group (PoCoG), University of Sydney  
President, COSA

**Professor David Thomas**  
Director, The Kinghorn Cancer Centre, Conjoint Professor, St Vincent’s Clinical School, Faculty of Medicine, UNSW

**Professor Mathew Vadas AO, FAHMS**  
Executive Director, Centenary Institute for Cancer Medicine and Cell Biology

**Professor Jane Young**  
Executive Director, Research, RPA Institute of Academic Surgery, Sydney Local Health District (SLHD)  
Executive Director, Surgical Outcomes Research Centre (SOuRCe), SLHD and University of Sydney  
Professor in Cancer Epidemiology, Sydney School of Public Health, University of Sydney

**Dr Karen Briscoe**  
Medical Oncologist, Mid North Coast Cancer Institute - Coffs Harbour Health Campus  
Lecturer, UNSW

**Associate Professor Philip Beale**  
Clinical Director of Cancer Services and Palliative Care for the Sydney Local Health District  
Head of Medical Oncology CRGH  
Associate Professor Medicine, Concord Clinical School  
Chair Sydney Catalyst T2T3 Working Group
Our Scientific Advisory Committee (SAC)

Chaired by Professor Butow, our SAC includes all members of GC plus:

**Professor Lisa Horvath**  
Inaugural director of research  
Professor of medical oncology (Genitourinary cancer) USyd  
Ass prof at UNSW  
Head of Clinical Prostate Cancer research Kinghorn

**Dr Nicole Rankin**  
Senior Research Fellow in lung cancer, Cancer Council NSW  
Sydney Catalyst Senior Translational Research Fellow, University of Sydney  
Chair Sydney Catalyst International Translational Cancer Research Symposium Organising Committee

**Dr Anthony Joshua**  
Head, Department of Medical Oncology, Kinghorn Cancer Centre,  
Conjoint Associate Professor, St Vincent’s Clinical School, UNSW

**Professor Susan Clark, FAA**  
Division Head - Genomics and Epigenetics ,Garvan Institute of Medical Research  
Senior Principal Research Fellow (NHMRC)  
Conjoint Professor, St Vincent's Clinical School, Faculty of Medicine, UNSW

**John Stubbs**  
Consumer Representative

**Dr Sonia Yip PhD**  
Sydney Catalyst Senior Translational Research Fellow, University of Sydney  
Translational Research Fellow and Oncology Translational Research Manager NHMRC Clinical Trials Centre.

**Associate Professor Peter Grimison**  
Staff Specialist in Medical Oncology at Chris O’Brien Lifehouse  
Visiting Medical Officer at Royal Prince Alfred and Dubbo Base Hospitals  
Clinical Senior Lecturer at the University of Sydney  
Chair Sydney Catalyst Scholarship Committee

**Professor Kate White**  
Professor Cancer Nursing, Cancer Nursing Research Unit (CNRU), Sydney Nursing School University of Sydney  
Co Chair Sydney Catalyst Pilot and Seed Committee

**Danielle Miller**  
Research Manager, Sydney Catalyst

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Sydney Catalyst Central Office:

Based within the NHMRC Clinical trials Centre at the Chris O’Brien Lifehouse, the Sydney Catalyst Central Office is mission control for our broad and diverse network. The team includes:

**Danielle Miller**  
Research Manager

**Dr Bea Brown**  
Program Manager, Embedding Research In Cancer Healthcare (EnRICH)

**Jaclyn Verghis**  
Research Coordinator, Embedding Research In Cancer Healthcare (EnRICH)

**Dr Henna Kuusisto**  
Technical Officer, Embedding Research In Cancer Healthcare (EnRICH)

**Penny Cannan**  
Communications Officer

**Carin Cinnadaio**  
Administration Assistant
I am very pleased to welcome you to the Sydney Catalyst International Translational Cancer Research Symposium. This is our third biennial Symposium and I’m sure that you’ll agree that Nicole Rankin and the rest of the organising committee have put together an excellent program.

Sydney Catalyst was established in July 2011 with a 5 year Translational Cancer Research Centre (TCRC) grant from the Cancer Institute NSW (CINSW), with the aim of improving outcomes for people affected by cancer. We successfully secured a second 5 year TCRC grant in mid-2016, enabling us to continue our work in facilitating and supporting a comprehensive research program, which as a whole is greater than the sum of its parts. Our consortium is a multi-disciplinary, multi-institutional endeavour that brings together outstanding teams of researchers and clinicians with expertise in translational research across the full continuum from basic biosciences, molecular biomarker discovery, descriptive research, clinical trials, psychosocial research and implementation research of best evidence-based care into practice.

In the 6 years since the centre was established, we’ve celebrated a number of important achievements, including;

- Growth in membership to more than 600 individual members from approx. 30 member groups and institutions.
- Developing and implementing a comprehensive research program through 3 flagship programs and ongoing facilitation and support of a broad range (over 100 formally) of member-led research projects.
- An extensive program of both face-to-face and virtual professional development, education and communication/networking events and resources to help our members grow and connect.
- Efforts to build capacity in research, including significant support and opportunities for early-mid career researchers and clinician-researchers specifically.
- Efforts to improve competitive advantage in securing other funds, including providing concept and grant development support to members.
- We have received an excellent rating against all assessment criteria in response to our last 4 annual progress reports to the CINSW. Most recently, the reviewers noted ‘Sydney Catalyst has an outstanding team and the Centre is clearly exceeding the requirements of the TCRC program...Sydney Catalyst should be proud of their impressive achievements as reported and they have made significant progress against all of the goals of the TCRC program’.

The success that we have enjoyed together is a testament to the commitment of our members. A special thanks to our Research Manager Danielle Miller and all our central office team who have developed and coordinated so much of the Sydney Catalyst enterprise. I am proud to be involved as the Director of Sydney Catalyst and encourage all of our members and collaborators to engage with us (and each other) actively and often to help ensure that we can continue to achieve our goals.

Professor John Simes
Director, Sydney Catalyst
August 2017

What are we doing well? What could we do more of?
TELL US: https://www.surveymonkey.com/r/sydneycatalyst
What We Do

We support and facilitate translational research. Our members have significant expertise across the translational research spectrum from basic biosciences, molecular biomarker discovery, descriptive research, clinical trials, psychosocial research and implementation research.

We have a range of multi-disciplinary, cross-institutional committees and working groups supporting new research and the implementation of evidence into practice. Sydney Catalyst supports top-down and bottom-up research initiatives and we offer a range of events and resources to help get our members moving.

How We Do It

We connect.

Sydney Catalyst facilitates communication and collaboration between the multiple disciplines and institutions that make up our membership.

We're here to introduce, unite and collaborate.

We're passionate about helping our members join forces to achieve common goals across the full spectrum of translational cancer research.
Our Research

Bench to Bedside:

Practice Based Research:

Evidence Into Practice:

The Translational Research Pipeline
Developing treatments and interventions –
The translation of basic wet and dry lab research into human research. A close link between bench & bedside allows new knowledge of disease to be developed into clinically relevant diagnostic & treatment regimens for human trials. Types of T1 studies/activities include observational studies, case studies, Phase I and II clinical trials, etc.

Translation to patients –
The translation of new clinical science and knowledge into routine clinical practice and health decision making. Types of T2 studies/activities include Phase III clinical trials, observational studies and survey research, evidence synthesis (incl. meta-analyses and systematic reviews), guidelines development, etc.

Translation to practice –
Dissemination and implementation research for system-wide change. Moving evidence from clinical trials and evidence-based guidelines into health practice, through delivery, dissemination and diffusion research. Types of T3 studies/activities include dissemination research, implementation research, diffusion research, Phase IV clinical trials, etc.
Our Activities

Sydney Catalyst facilitates communication and collaboration between the multiple disciplines and institutions that make up our membership. We’re here to introduce, unite and collaborate.

- Education Dinner Series Events
- Research, Education & Skills Workshops
- Members in Focus & Member Group Visits
- ‘EnRICH’ Embedding Research In Cancer Healthcare
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<tr>
<td>8:00 - 8:30</td>
<td>Registration - Chair: Dr Nicole Rankin</td>
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<td>8:30 - 8:40</td>
<td>Welcome + Introduction - Prof John Simes</td>
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<td>8:40 - 8:45</td>
<td>Welcome to Country - Uncle Chicka Madden</td>
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<td>8:45 - 9:05</td>
<td>Identifying areas of need in order to improve cancer outcomes</td>
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<td>Prof David Currow, CEO CINSW</td>
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<td>9:05 - 10:30</td>
<td>Session One - Chair: Prof Lisa Horvath</td>
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<td>9:05 - 9:40</td>
<td>Keynote 1: Cancer with Poor Outcomes: Lessons from Advanced Melanoma</td>
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<td>Prof Grant McArthur</td>
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<td>9:40 - 10:00</td>
<td>Plasma-activated nanoparticles for nucleic acid drug delivery</td>
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<td>Assoc Prof Glen Reid and Prof David McKenzie</td>
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<td>10:00 - 10:15</td>
<td>Implementing clinical cell &amp; gene therapies for cancer</td>
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<td>Prof John Rasko</td>
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<td>10:15 - 10:30</td>
<td>Making screening, assessment, referral and management of anxiety and depression in cancer care a reality: developing a system addressing barriers and facilitators to support sustainable implementation (The ADAPT Program)</td>
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<td>Dr Jo Shaw</td>
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<td>10:30 - 11:00</td>
<td>Morning Tea</td>
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<td>11:00 - 11:15</td>
<td>Session Two - Chair: Prof Jane Young</td>
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<td>11:00 - 11:35</td>
<td>Keynote 2: From T3 to T4: Another valley of death?</td>
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<td>Prof Janet Hiller</td>
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<td>11:35 - 11:55</td>
<td>Radiation - the other chemotherapy drug - Frontiers in physics and radiotherapy research, with a focus on the new developments that are likely to make a real difference for patients.</td>
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<td>11:55 - 12:10</td>
<td>The Effect of Exercise in combination with chemotherapy on breast cancer tumour biology, immunology and vascularisation - a non-pharmaceutical approach to current oncology treatment?</td>
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<td>Dr Sara Wahlroos</td>
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   *Prof Derek Hart* |
   *Ms Merran Findlay* |
| 12:40 - 1:15 | KEYNOTE 3: Impediments and cost considerations for translation of molecular prognostication  
   *Prof Derek Raghavan* |
| 1:15 - 2:15 | **LUNCH + POSTER VIEWING** |
| 2:15 - 4:30 | **SESSION THREE - Chair: Prof Phil Hogg**  
   **2:15 - 3:15** | Panel discussion: 'Future frontiers in funding - innovation, translation, commercialisation and public good.'  
   *Facilitated by Julie McCrossin.*  
   **3:15 - 3:30** | Embedding Research (and Evidence) in Cancer Healthcare - EnRICH  
   *Prof Michael Boyer*  
   **3:30 - 3:45** | Effect sizes hypothesized and observed in contemporary phase 3 trials of targeted and immunological therapies for advanced cancer  
   *Dr Nicky Lawrence*  
   **3:45 - 4:00** | Preclinical development of glutamine transport inhibitors as novel therapies in melanoma, breast and prostate cancers  
   *Assoc Prof Jeff Holst*  
   **4:00 - 4:15** | Translating cancer genomics to the clinic, for advanced childhood and rare adult cancers  
   *Dr Mark Cowley*  
   **4:15 - 4:25** | Facilitated poster discussion and prizes.  
   *Julie McCrossin and Dr Nicole Rankin*  
   **4:25 - 4:30** | Wrap up, evaluations, and thank yous.  
   *Dr Nicole Rankin*  
   **4:30 - 5:30** | **DRINKS + CANAPES TO FINISH** |
Welcome

Dr Nicole Rankin
Senior Research Fellow
Sydney Catalyst and Cancer Council NSW
As Chair of the Sydney Catalyst International Translational Cancer Research Symposium, it gives me great pleasure to welcome you to this, our third Symposium. The Sydney Catalyst Governing Council, led by Director Professor John Simes, along with the Scientific Advisory Committee and members of this year’s Organising Committee, are delighted that you have chosen to participate.

Sydney Catalyst aims to improve health outcomes for all people affected by cancer. Over the past six years, we have built a comprehensive translational research program to address that aim. Our members have vast expertise in translational research across the full continuum from basic biosciences, molecular biomarker discovery, clinical trials, health services and epidemiology, nursing, psychosocial research and implementation science.

The program theme, Frontiers in Translation, was chosen by the Organising Committee as it captures the challenges we face as researchers and clinicians to extend the boundaries of scientific knowledge and ensure knowledge is translated to maximize benefits for all.

The program features a fantastic group of presenters. Our keynote speakers, Grant McArthur, Janet Hiller and Derek Raghavan bring a wealth of international and national experience across the translational spectrum. The oral presentations from across our membership and invited guest, Martin Ebert, will offer something for everyone. We are also excited to welcome the dynamic and inspiring Julie McCrossin, as our panel facilitator.

The Committee and I hope that the Symposium will exceed your expectations. Please take the opportunity to network, extend a hand to new members and start a conversation about your work and translational passions.

A big thank you to the Organising Committee members: Natalka Suchowerska, Alex Swarbrick, Puma Sundaresan, Phil Waddock, Mainthan Palandira, David McKenzie and Danielle Miller.

We hope you enjoy the day.
SYMPOSIUM ORGANISING COMMITTEE

Dr Nicole Rankin (Chair)
Senior Research Fellow in lung cancer, Cancer Council NSW
Sydney Catalyst Senior Translational Research Fellow, University of Sydney

Prof. David McKenzie
Professor of Materials Physics, University of Sydney

Danielle Miller
Research Manager, Sydney Catalyst

Dr Mainthan Palendira
Head of Human Viral & Cancer Immunology Laboratory, Centenary Institute

A/Prof Natalka Suchowerska
Head of Physics Research and Education, The Chris O’Brien Lifehouse

Dr Puma Sundaresan
Staff Specialist Radiation Oncologist, Crown Princess Mary Cancer Centre
Clinical Senior Lecturer, University of Sydney

A/Prof Alex Swarbrick
Lab Head - Tumour Progression, Senior Research Fellow, Garvan Institute of Medical Research
Conjoint Associate Professor, St Vincent’s Clinical School, Faculty of Medicine, UNSW Sydney

Phil Waddick
Consumer Representative

KEYNOTE SPEAKERS

**Professor Grant McArthur**
Fellow of the Royal Australasian College of Physicians and holds a Ph.D. in Medical Biology, Prof. McArthur is the Executive Director of the Victorian Comprehensive Cancer Centre and the inaugural Lorenzo Galli Chair of Melanoma and Skin Cancers at the University of Melbourne. His awards include the inaugural winner of the Translational Research Award of the Foundation Nelia et Amadeo Barletta, the Sir Edward Dunlop Clinical Cancer Research Fellowship of the Cancer Council of Victoria and the inaugural Martin Lackmann medal for translational research. He is national and international study Co-Chair of a number of clinical trials of targeted therapies. His research Interests include discovery of novel drug targets in cancer, targeting oncogenes, clinical trials of targeted therapeutics, personalised medicine, melanoma, cell cycle control, metabolism and protein synthesis in cancer, and functional imaging. Professor McArthur is on the Editorial Boards of Annals of Oncology, Anti-Cancer Drugs, the Journal of Clinical Oncology, the Open Clinical Cancer Journal, Therapeutic Advances in Medical Oncology and the Journal of Personalised Medicine. He has published over 200 papers including senior or first author publications in the following journals: New England Journal of Medicine, Journal of Clinical Oncology, Lancet Oncology, Cancer Discovery, Cancer Cell, Nature Cell Biology, Blood and EMBO.

**Professor Derek Raghavan**
Prof Raghavan is President of Levine Cancer Institute and former Chair and Director of Cleveland Clinic Taussig Cancer Institute. Research interests include genitourinary oncology, value in oncology, geriatric oncology and molecular prognostication. Graduate of University of Sydney (MBBS 1974, MD 2012), University of London (PhD 1984), 300 publications, 12 books.

**Professor Janet Hiller**
Professor Janet Hiller is Dean of the School of Health Sciences in the Faculty of Health, Arts and Design, Swinburne University. She is an epidemiologist and health services researcher with an interest in the use of evidence in policy and practice, health technology assessment and socially informed innovation.
“Identifying areas of need in order to improve cancer outcomes”

Professor David Currow
Chief Cancer Officer, NSW and Chief Executive Officer, Cancer Institute NSW, the NSW Government’s cancer control agency. He was appointed to the position in March 2010. Prior to this, he was the foundation Chief Executive Officer of Cancer Australia, the Commonwealth’s cancer control agency.

ABSTRACT: Cancer outcomes continue to improve from a combination of factors: in some cases earlier diagnosis; better staging through advanced imaging and better defining other prognostics factors; new therapies; and improved overall health in the community.

The improvements seen across the population which are now associated with 70% five year survival for all people diagnosed with cancer potentially hides the fact that there are identifiable groups within the community where those outcomes are not being achieved. Although for each of those communities, there is an improvement in outcomes there is still a substantial gap.

These communities include people from Aboriginal and Torres Strait Islander backgrounds, people from some Culturally and Linguistically Diverse communities, people from lower socio economic strata, and people from rural and remote communities. Several of these factors may overlap in a single person and have an impact on cancer outcomes.

Ultimately, cancer services need to understand the specific opportunities to close these gaps in cancer outcomes and drive improved care across the whole community. This is a key challenge for the next decade of cancer control in Australia.

“Cancer with poor outcomes: lessons from advanced melanoma”

Professor Grant McArthur
Executive Director, Victorian Comprehensive Cancer Centre

BIO: Fellow of the Royal Australasian College of Physicians and holds a Ph.D. in Medical Biology, Prof. McArthur is the Executive Director of the Victorian Comprehensive Cancer Centre and the inaugural Lorenzo Galli Chair of Melanoma and Skin Cancers at the University of Melbourne. His awards include the inaugural winner of the Translational Research Award of the Foundation Nelia et Amadeo Barletta, the Sir Edward Dunlop Clinical Cancer Research Fellowship of the Cancer Council of Victoria and the inaugural Martin Lackmann medal for translational research. He is national and international study Co-Chair of a number of clinical trials of targeted therapies. His research Interests include discovery of novel drug targets in cancer, targeting oncogenes, clinical trials of targeted therapeutics, personalised medicine, melanoma, cell cycle control, metabolism and protein synthesis in cancer, and functional imaging. Professor McArthur is on the Editorial Boards of Annals of Oncology, Anti-Cancer Drugs, the Journal of Clinical Oncology, the Open Clinical Cancer Journal, Therapeutic Advances in Medical Oncology and the Journal of Personalised Medicine. He has published over 200 papers including senior or first author publications in the following journals: New England Journal of Medicine, Journal of Clinical Oncology, Lancet Oncology, Cancer Discovery, Cancer Cell, Nature Cell Biology, Blood and EMBO.
“Plasma-activated nanoparticles for nucleic acid drug delivery”

Associate Professor Glen Reid
Senior Scientist at the Asbestos Diseases Research Institute (ADRI)

Professor David McKenzie
Professor of Materials Physics, University of Sydney

BIO: A/Prof Reid’s research focuses on the asbestos-related cancer malignant pleural mesothelioma, and aims to identify new biomarkers and novel molecular targets. His group has identified a number of microRNAs that are candidate tumour and blood biomarkers, and recently completed a phase I trial of a microRNA-based therapy in mesothelioma patients.

Professor McKenzie’s research focuses on the production of new materials and new processes for creating them. The group is developing methods originating from plasma physics for binding biomolecules onto surfaces. A particular focus is the covalent binding of nucleotides and antibodies onto nanoparticles for delivery of cancer therapeutics and cancer diagnostics. The aim is to produce technology for a “universal nanoparticle” that can be customized for individual treatments.

ABSTRACT: Gene silencing drugs based on siRNAs and microRNAs have enormous potential in the treatment of cancer, as they can be used to specifically control target genes based on sequence-dependent interactions. Despite their promise, however, delivery of these molecules to target cells remains a major hurdle. Naked siRNA is negatively charged and therefore does not penetrate cell membranes, is readily degraded by serum nucleases, and is quickly eliminated by renal secretion. We have found that plasma immersion ion implantation (PIII) can be used to activate surfaces so that they present appropriate charge and hydrophilicity to cell membranes and simultaneously form covalent bonds with biomolecules, including peptides, oligonucleotides and siRNAs. In this project we aim to construct nanoparticles (NPs) functionalized with multiple biomolecules to allow specific delivery of cargo to cancer cells. By combining targeting peptides or antibodies with siRNAs or microRNAs on the same nanoparticle we aim to specifically deliver siRNAs and microRNAs to cancer cells in vitro and in vivo. This innovative approach has the potential to be a gateway technology leading to a truly personalized therapy, as the same PIII-activated nanoparticles can be functionalized with an unlimited range of targeting moieties and nucleic acids without changing the process.

“Implementing clinical cell & gene therapies for cancer”

Professor John Rasko AO
Head of Department, Cell & Molecular Therapies, Royal Prince Alfred Hospital

BIO: Professor Rasko is an Australian pioneer in the application of adult stem cells and genetic therapy. He directs the Department of Cell and Molecular Therapies at Royal Prince Alfred Hospital and heads the Gene and Stem Cell Therapy Program at the Centenary Institute, University of Sydney.

John Rasko is a clinical haematologist, pathologist and scientist with an international reputation in gene and stem cell therapy, experimental haematology and molecular biology. In over 150 publications he has contributed to the understanding of stem cells and haemopoiesis, gene transfer technologies, oncogenesis, human genetic diseases and non-coding RNAs.

He serves on Hospital, state and national bodies including Chair of GTTAC, Office of the Gene Technology Regulator – responsible for regulating all genetically-modified organisms in Australia - and immediate past Chair of the Advisory Committee on Biologicals, Therapeutic Goods Administration. Contributions to scientific organisations include co-founding (2000) and past-President (2003-5) of the Australasian Gene Therapy Society; Vice President (2008-12) and
President-elect (2016-17) International Society for Cellular Therapy; Scientific Advisory Committees and Board member for philanthropic foundations; and several Human Research Ethics Committees. He is a founding Fellow of the Australian Academy of Health and Medical Sciences. He is the recipient of national (RCPA, RACP, ASBMB) and international awards in recognition of his commitment to excellence in medical research, including appointment as an Officer of the Order of Australia.

**ABSTRACT:** Emerging cell and gene therapies designed to target the treatment of cancer require controlled development in compliance with safety, regulatory and GMP requirements. Since 2000 the Department of Cell & Molecular Therapies at RPAH has undertaken early-phase clinical trials in haemophilia, thalassaemia, GVHD and haematological malignancies. The challenges of undertaking multi-centre trials will be discussed in the context of the pivotal multi-center JULIET study (NCT02445248). Recent interim results of this Phase II trial using CTL019 CAR-T cells has demonstrated durable complete responses in adults with relapsed or refractory Diffuse Large B-Cell Lymphoma. The three-month overall response rate was 45%, with 37% exhibiting a complete response. Since CAR-T cells are manufactured for each individual patient using their own cells, this new type of medicine presents novel challenges to be discussed. While legitimate advances are being made in cellular immunotherapies, medical and, in particular, stem cell tourism has become a billion dollar industry with increasing examples of false claims. Unregulated, untested or unsafe stem cell ‘therapies’ place the field at a difficult crossroad. Blurring the lines that distinguish evidence-based stem cell therapies from those that are not remains a fundamental public health concern.

“Making screening, assessment, referral and management of anxiety and depression in cancer care a reality: developing a system addressing barriers and facilitators to support sustainable implementation (The ADAPT Program)”

**Dr Jo Shaw**
Executive Director, Senior Research Fellow, Psycho-oncology Co-operative Research Group (PoCoG)

**BIO:** Dr Shaw is a psycho-oncology and health communication researcher. She has played a pivotal role in developing and implementing the Australian Clinical Pathway for managing depression and anxiety in cancer. Combining her academic psychology and health services research experience, Dr Shaw’s current research focus is alternative treatment delivery models, quality and costs of evidence-based psycho-oncology interventions.

**ABSTRACT:** Background: Clinical pathways have shown considerable success in bringing about change in patient management, however the context and implementation strategies utilised are critical. The Clinical Pathway for the Identification and Management of Anxiety and Depression in Adult Cancer Patients (Clinical Pathway) advocates routine screening across the cancer journey, promoting early identification and prompt access to evidence-based care as well as educational support of cancer care staff to guide appropriate and successful implementation.

**Methods & Results:** Our barrier analysis identified lack of resources, education and training and support from leaders; poor uptake by patients; and lack of integration within the community, as key. The Anxiety and Depression Pathway (ADAPT) research program in Australia has developed a suite of resources addressing these barriers and facilitators. These include: (i) the ADAPT Portal, a flexible web-based system to operationalise the stepped care model incorporated into the Clinical Pathway for individual cancer services, recommendations for validated screening tools and evidence-based interventions for identifying and managing anxiety and depression; (ii) an online health professional training program focusing on skills related to screening and discussion about referral with patients; (iii) a purpose-built online CBT-based therapy program for managing anxiety/depression in the cancer context, iCanADAPT; and (iv) patient resources to inform, normalise and de-stigmatise routine screening and managing the impact of cancer on emotional wellbeing.

**Conclusion:** Lessons learned from pilot testing of these resources, ahead of the planned cluster RCT of implementation strategies in 12 cancer services in NSW, will be presented and discussed.

**Funding:** Cancer Institute NSW
“From T3 to T4: Another valley of death?”

**Professor Janet Hiller**  
Dean, School of Health Sciences, Swinburne University of Technology

**BIO:** Professor Janet Hiller is Dean of the School of Health Sciences in the Faculty of Health, Arts and Design, Swinburne University. She is an epidemiologist and health services researcher with an interest in the use of evidence in policy and practice, health technology assessment and socially informed innovation.

**ABSTRACT:** The focus of many translational research initiatives has been on moving innovations from the bench to the bedside. The additional move from practice, often in individual health settings such as single hospitals or networks, into population health impact has additional challenges. The roles of evidence, context, reimbursement processes and theory in upscaling evidence for population health impact, will be examined in relation to two case studies. The systematic review of clinical effectiveness and safety is a starting point and one component of the evidentiary requirements for upscaling. Analysis of the values and voices of stakeholders including clinicians, patients, citizens and policy makers along with the health ecosystem in which the innovation is to be implemented all have an impact on the likelihood of translation. Ensuring population access to health innovations requires sound, fair processes for reimbursement. Social science is an adjunct to basic science and clinical research in the journey from bench to bedside to populations.

“Radiation - the other chemotherapy drug: Frontiers in physics and radiotherapy research, with a focus on the new developments that are likely to make a real difference for patients.”

**Professor Martin Ebert**  
Director of Physics Research in Radiation Oncology, Sir Charles Gairdner Hospital

**BIO:** Martin Ebert is a physicist who has worked in cancer therapy for over 20 years, providing clinical support, managing services and undertaking translational research. He currently works in Perth where he leads a research program focused on translation of clinical trials data and in examining the fundamental physics of cancer.

**ABSTRACT:** Physicists have contributed extensively to medicine, providing the groundwork for most, if not all, diagnostic imaging modalities. They have contributed to cancer therapy primarily through development and application of radiation delivery devices, and all contemporary radiotherapy centres are now supported by a contingent of medical physicists. The classical model for the action of radiation involves ‘direct’ spatial targeting of cells and the ability to spatially-localise radiation delivery is still a primary focus for physicists researching in radiotherapy. However, evidence from the last decade suggests that the direct killing of cancer cells is only a part, and possibly not the main part, of how radiation can be used for therapeutic effect in oncology. Radiation is now seen as an agent that can modify the tumour microenvironment, impacting on vessels either directly or by modulating angiogenesis, inducing cell signalling, stimulating and facilitating immune response. These mechanisms lead to ‘non-direct’ or ‘facilitated’ killing of cancer cells, potentially even systemic effects. We will examine such effects, how they may be capitalised upon by drug-based strategies, and how the oncology community can engage with physicists and mathematicians to ensure the related translational research can be undertaken.
“The Effect of Exercise in combination with chemotherapy on breast cancer tumour biology, immunology and vascularisation - a non-pharmaceutical approach to current oncology treatment?”

Dr Sara Wahlroos
Breast Oncology Fellow, The Kinghorn Cancer Centre. PhD Student, The Garvan Institute of Medical Research

BIO: Dr Wahlroos is a Medical Oncology Fellow at the Kinghorn Cancer Centre, and has embarked on a PhD this year at The Garvan Institute of Medical Research. She has an interest in survivorship and in particular the impact of exercise on breast cancer.

ABSTRACT: The beneficial role of exercise following a cancer diagnosis is increasingly recognised as an important lifestyle modification. The suggested mechanisms for the therapeutic role of exercise in delaying cancer recurrence and mortality are still under investigation. The aim of this project is to determine the metabolic pathways, the impact of the immune system, as well as tumour blood flow as a response to exercise, with or without anti-cancer treatment, in pre-clinical models of breast cancer subtypes. In parallel to the pre-clinical work, we will run a small pilot study looking at the feasibility of exercising directly after neoadjuvant chemotherapy in women with early breast cancer. With the help of our feasibility study, we aim to show that there is a translational link between outcomes in pre-clinical models and clinical models. We aim to develop robust clinical evidence for the beneficial effects of exercise in breast cancer in a larger trial, with the long-term goal to integrate exercise as part of systemic treatment prescription.

“Immune Therapies: the Second Wave.”

Professor Derek Hart
Head, Dendritic Cell Biology and Therapeutics Group, Professor of Transplantation and Immunotherapy, ANZAC Research Institute, Concord Clinical School

BIO: Derek leads the Dendritic Cell Research group which is a part of the ANZAC Research Institute at the University of Sydney. Derek is a Rhodes Scholar and RCPA Distinguished Fellow. Prior to this Derek, directed the Christchurch Clinical Haematology Unit and BMT Unit; completed 11 years as the inaugural Mater Medical Research Institute Director in Brisbane and his leadership helped create the new Queensland Translational Institute.

ABSTRACT: The concept that immune therapies might cure cancer began with Coley’s toxins. Our early investigations showed that the immune system alone could irradiate leukaemia (Hill et al. Pathology 1996;28:51) and that dendritic cells (DC) as the specialist antigen presenting cells could generate highly specific T cell responses to a leukaemia specific mutation (Mannering et al Blood 1997;90:290). Fast forward 20 years and now immune therapies, notably monoclonal antibodies (mAbs) to the checkpoint inhibitors, chimeric antigen receptor (CAR) T cells, Bi specific T cell Engagers (BiTes) and other mAb derivatives are curing patients. Research is raising the possibility that chemotherapy and radiotherapy may generate curative anti-cancer immune responses.

Our group has focused on studying DC and their surface molecules using mAbs to define new targets that allow us to study fundamental DC and cell biology that may generate new immune strategies. Our translational program explores the diagnostic and therapeutic potential of these molecules. The presentation will discuss therapeutic prospects for immune therapy targeting the CD83, CD302, CD300 molecules and a “second generation” DC vaccine.

Ms Merran Findlay
Executive Research Lead – Cancer Nutrition and Oncology Specialist Dietitian, Royal Prince Alfred Hospital/Chris O’Brien Lifehouse

BIO: Merran is the Executive Research Lead-Cancer Nutrition and Oncology Specialist Dietitian across the Royal Prince Alfred Hospital-Chris O’Brien Lifehouse partnership. She was awarded an NHMRC TRIP Fellowship to implement an innovative model of nutrition care for patients with head and neck cancer.

ABSTRACT: Aims: Malnutrition is prevalent in patients with head and neck cancer (HNC) impacting on outcomes. Despite publication of evidence-based nutrition guidelines (EBGs), significant evidence-practice gaps exist. This project aims to implement and evaluate a best-practice dietetic model of care (MOC) based upon the best-available evidence to minimise the detrimental sequelae of malnutrition.

Methods: A mixed methods, pre- and post- implementation of the new MOC. Qualitative interviews were conducted with consumers and clinicians to identify barriers and facilitators to change. Medical record audit established baseline adherence to best practice recommendations and clinical parameters prior to implementation in a prospective cohort. Focus groups with were conducted to evaluate MDT members’ feedback on the new MOC.

Results: Thirty interviews conducted with consumers (n=11) and clinicians (n=19) combined with clinical audit (n=98) revealed barriers and enablers at the individual, team and system levels, suggesting nutrition care is focussed on reactive rather than proactive management of those with greatest need. Reasons included lack of familiarity with EBGs, dietetic resource and infrastructure limitations and lack of awareness of the intensive nutrition care required. Forty-five per cent of unplanned admissions were due to nutrition-related morbidity for which economic evaluation revealed significant system-level impact. Post implementation data (n=34) indicate improved adherence to process measures: pre-treatment dietitian assessment 20% to 97%; use of validated nutrition assessment tools before (83% to 100%), during (4% to 82%) and after treatment (6% to 90%). Impact on clinical outcomes is under evaluation. Preliminary analysis suggests a positive impact on cost outcomes while focus groups demonstrated clear support for continuing the new MOC.

Conclusions: This project demonstrates a systematic approach to implementing effective strategies for a new MOC in HNC nutrition. The results provide justification for translation of an evidence-based MOC to and may be transferrable to other tumour groups and other health conditions.

Impediments and cost considerations for translation of molecular prognostication

Professor Derek Raghavan
President, Levine Cancer Institute, Carolinas HealthCare System

BIO: Prof Raghavan is President of Levine Cancer Institute and former Chair and Director of Cleveland Clinic Taussig Cancer Institute. Research interests include genitourinary oncology, value in oncology, geriatric oncology and molecular prognostication. Graduate of University of Sydney (MBBS 1974, MD 2012), University of London (PhD 1984), 300 publications, 12 books.

ABSTRACT: The greatest progress in oncology in decades has involved the development of tools of molecular diagnosis, prediction and prognostication. Initial molecular studies were expensive and the per unit costs have reduced. However, commercialization and scaling to the volumes required for cancer trials have become prohibitively expensive. Many of the postulated molecular associations are unproven and thus reimbursement for large scale testing is extremely challenging. Further, many clinicians are poorly trained in molecular oncology. Scalable strategies to address these issues are discussed.
SESSION 3
Chair: Professor Phil Hogg

PANEL DISCUSSION
“Future frontiers in funding - innovation, translation, commercialisation and public good.”

Facilitated by Julie McCrossin
BIO: Julie McCrossin gets people talking and she is renowned for her warmth, humour, intelligence and commitment to social justice.

After 20 years as a broadcaster with ABC Radio National, ABC TV and Network Ten, she is now a freelance journalist and facilitator. She presented the radio show Life Matters on ABC Radio National for 5 years, covering countless health, welfare and educational topics with a frequent rural focus. Julie was also a team leader on the media quiz show “Good News Week” for 5 years on Network Ten and ABC TV.

Currently Julie writes for the NSW Law Society Journal and facilitates conferences and seminars nationally. Julie offers a range of interactive formats that stimulate audience discussion while keeping people on topic and on time. Julie is especially known for her capacity to guide forums on sensitive topics, such as suicide prevention, mental health, child protection and family law.

Julie has qualifications in the arts, education and law. She is an Ambassador for Targeting Cancer and TROG Cancer Research.

ON STAGE PANELLISTS:
Derek Raghavan (President, Levine Cancer Institute, Carolinas HealthCare System)
Grant McArthur (Executive Director, Victorian Comprehensive Cancer Centre)
Janet Hiller (Dean, School of Health Sciences, Swinburne University of Technology)
Phyllis Butow (Professor and NHMRC Senior Principal Research Fellow in the School of Psychology, USYD)

“Embedding Research (and Evidence) in Cancer Healthcare - EnRICH”

Professor Michael Boyer
Chief Clinical Officer, Chris O’Brien Lifehouse, EnRICH Clinical Lead

BIO: Michael is a medical oncologist with a major clinical interest in the treatment of thoracic and head and neck cancers. In 2010, he was made a member of the Order of Australia for his work as an educator, a clinical trials researcher and his involvement in the development of integrated care facilities for people suffering with cancer. His current research focuses on the testing of new anticancer drugs for the treatment of lung cancer.

ABSTRACT: Lung cancer is the most common cause of cancer death in Australia, accounting for nearly 20% of all cancer deaths, and is a leading cause of morbidity and burden of disease. The outlook for patients with lung cancer is poor, with only a 15% overall five year survival rate. For patients diagnosed with advanced stage disease, five year survival decreases to 1%. Improvements in lung cancer survival rates are not comparable with improvements for other cancers.
The Sydney Catalyst EnRICH program, will build a program of research in lung cancer to develop and extend evidence of effective treatments and to increase the use of clinical care based on existing evidence. EnRICH will assemble a prospective cohort of 1000 patients to: describe the natural history of and patterns of care for lung cancer; identify current gaps in evidence and practice for clinical quality improvement; create a platform for researchers across the T1-T3 translational research spectrum to develop and initiate clinical research and intervention studies to address gaps. EnRICH will include matched demographic, clinical, biomarker, molecular profile, and outcome data (including quality of care and patient-reported outcomes), in addition to archival biopsy tissue and serial blood samples for current and future research projects.

“Effect sizes hypothesized and observed in contemporary phase 3 trials of targeted and immunological therapies for advanced cancer”

Dr Nicky Lawrence
Oncology Research Fellow and PhD Candidate, NHMRC Clinical Trials Centre, University of Sydney

BIO: Dr Lawrence is a Medical Oncologist working at the NHMRC Clinical Trials Centre as a part-time research fellow for the Australian and New Zealand Urogenital and Prostate Cancer Trials Group, as well as undertaking a PhD at the University of Sydney. She has an interest in genitourinary malignancies and clinical trial design.

ABSTRACT: The general aim of Dr Lawrence’s PhD is to determine the optimal methods for clinical trials testing novel, targeted anticancer drugs. One of the specific objectives is to determine the magnitudes of effect sizes hypothesised and effect sizes observed, and their relationship, in phase 3 trials of targeted and immunological therapies in advanced cancers.

“Preclinical development of glutamine transport inhibitors as novel therapies in melanoma, breast and prostate cancers”

Associate Professor Jeff Holst
Head of Origins of Cancer Program, Centenary Institute

BIO: A/Prof Jeff Holst is a Faculty member at the Centenary Institute, and a Conjoint Associate Professor at the University of Sydney. His laboratory is focussed on understanding amino acid metabolism in cancer, and is developing novel drugs to target amino acid uptake in melanoma, breast and prostate cancer.

ABSTRACT: Cancer cell metabolism has recently been added to the original six Hallmarks of Cancer. This reflects a renewed appreciation of the Warburg effect, whereby cancer cells undergo a metabolic shift toward aerobic glycolysis, resulting in decreased energy production from glucose. The cancer cell’s energy and nutrition needs are subsequently replaced by an increased reliance on the metabolism of amino acids such as glutamine, a process driven by the oncogenic transcription factor MYC as well as adaptive responses to nutrient stress. This amplification of glutamine metabolic pathways leads to glutamine addiction in cancer cells. This provides attractive new therapeutic targets such as glutaminase, which is currently being targeted in clinical trials. Over the past few years, we have shown that melanoma, prostate cancer and triple-negative breast cancer cells upregulate the glutamine transporter ASCT2 to sustain their increased requirement for glutamine. Chemical inhibition or genetic knockdown of ASCT2 blocks glutamine uptake in these cancers, as well as downstream glutamine metabolism, suggesting that targeting ASCT2 is a viable therapeutic strategy. We have now developed a partnership with CSIRO, funded by the Medical Research Commercialisation Fund and Uniseed, to develop compounds that target glutamine transport in these cancers.
"Translating cancer genomics to the clinic, for advanced childhood and rare adult cancers"

Dr Mark Cowley
Head of Cancer Genomics, Garvan’s Kinghorn Centre for Clinical Genomics, Mid-career fellow, NSW Department of Health.

BIO: Dr Mark Cowley is the head of cancer genomics in Garvan’s Kinghorn Centre for Clinical Genomics, and a mid-career fellow with NSW Department of Health. His team is leading the development of precision cancer genomics approaches to characterise patient tumours with advanced, and/or rare cancers.

ABSTRACT: The comprehensive identification of genetic alterations in patient tumours offers the opportunity to substantially improve patient care, though identifying optimal therapies, obtaining a more precise diagnosis, and identifying inherited cancer risk variants. Through the efforts of TCGA and ICGC, comprehensive catalogues of mutations in the major cancer types are being developed, and linked to drug sensitivities through retrospective and prospective analyses of patients with exceptional responses. Patients with rare (collectively 30% of cancer deaths), or advanced cancers stand to benefit substantially from a genome-guided approach, whereby proven genotype-drug combinations from well-studied cancers can be translated to patients with cancers that are otherwise under-served.

In practice though, precision cancer genomics remains challenging, with many obstacles to overcome. These include developing the optimal ways to analyse and interpret individual patient cancer genome data, and many logistical challenges relating to sample acquisition, and meeting clinically relevant timeframes.

We will present our experience from recruiting over 250 patients this year into two genome-guided precision medicine programs in Australia. The Molecular Stratified Therapeutics trial (MoST) is enrolling patients with rare, and advanced cancers, and the Lions Kids Cancer Genome Project (LKCGP) is enrolling kids with advanced cancers.

Mark Cowley, John Grady, Marie Wong, Velimir Gayevskiy, Mark Pinese, Paulette Barahona, Emily Mould, Amit Kumar, Subotheni Thavaneswaran, Mandy Ballinger, Paul Eckert, Dong-Anh Quang, Vanessa Tyrrell, Michelle Haber, Glenn Marshall, Dominique Hess, Joe Collins, David Thomas, Marcel Dinger on behalf of the Lions Kids Cancer Genome Project, the Zero Childhood Cancer Program, and the Molecular Stratified Therapeutics Program.
“A systematic review of patient decision aid effectiveness: Is health-related quality of life (HRQOL) a suitable endpoint?”

AUTHOR(S): Claudia Rutherford, Madeleine King; Intissar Souli; Dawn Stacey
POSTER LOCATION: H1.3
ABSTRACT: Background: Patient decision aids (DAs) are interventions to help patients explore their treatment options and personal preferences. Some trials assess DA effectiveness with HRQOL measures. However, using HRQOL endpoints to determine DA effectiveness may not be suitable. We review how randomized controlled trials (RCTs) evaluating DA effectiveness measure and report HRQOL, and evaluate the effect of DAs on HRQOL.

Methods: We reviewed RCTs included in the 2014 Cochrane Review of DAs. Eligible trials assessed HRQOL at baseline and after DA use, and compared HRQOL between DA and comparison groups. Two reviewers assessed study quality independently. Analysis was descriptive.

Results: Of 115 RCTs, 11 (10%) measured HRQOL. All described baseline characteristics and reported HRQOL results. However, most studies failed to: state a priori HRQOL outcome expectations or hypotheses (64%); make a link between HRQOL and decisions (82%); provide a rationale for HRQOL assessment (82%); justify their choice of assessment time-points (91%); or adjust p-values for multiple domains and time points (100%). Patients randomised to DA interventions did not report better HRQOL than those in usual care groups.

Conclusion: When using HRQOL outcomes, DA effectiveness trials fail to describe rationales about why and how HRQOL has been assessed. It is unclear whether this is due to limitations in reporting or in study planning. Therefore, whether HRQOL is a suitable endpoint for DA effectiveness trials and the effect of DAs on HRQOL in the short- and long-term needs further exploration. Future DA research needs careful consideration of why and how HRQOL is assessed.


“Can the therapeutic benefits of microbeam radiation therapy be achieved using a clinical linac?”

AUTHOR(S): Natalka Suchowerska, Valery Peng, A. Dos Santos Esteves, Linda Rogers, Elizabeth Claridge Mackonis, David R. McKenzie
POSTER LOCATION: V1.2
ABSTRACT: High definition multileaf collimators (HDMLCs) with 2.5mm leaves provide an opportunity for ‘grid’ therapy to approach Microbeam Radiation Therapy (MRT). However, periodic spatial modulation of the dose in the target volume runs counter to current clinical practice. To optimize the modulation, a better understanding of cell dose responses to such treatments is needed. The aim of this study is to determine if the therapeutic benefits of MRT can be achieved using a clinical linac and to develop a predictive model to optimize the benefits.

Varian NovalisTxTM HD120-MLCs were used to generate grid patterns with 2.5mm and 5.0mm open stripes. Clonogenic survival of normal (HUVEC) and cancer (lung NCI-H460, breast HCC-1954, melanoma MM576) cell lines were compared in vitro for the same average dose, following irradiation with periodically modulated and open 6MV photon fields. Radiation field modulation did not affect the survival of normal cells, but for the same average dose, cancer cell survival was significantly lower for 2.5mm stripe-modulation and marginally so for 5.0mm stripe-modulation.

A mathematical model was developed to incorporate the dose gradients of the spatial modulation into the standard linear quadratic model. Our new extended bystander LQ model assumes spatial gradients drive the diffusion of soluble factors that influence survival through bystander effects and successfully predicts the experimental results that show an increased therapeutic ratio.

Our results challenge conventional radiotherapy practice and predict that additional gain could be realized by prescribing spatially modulated treatments to harness the bystander effect.
“CD103+ tumour-resident CD8+ T cells are a prognostic factor for survival in untreated metastatic melanoma and respond to immunotherapy”

AUTHOR/S: Jarem Edwards; James Wilmott; Jason Madore; Tuba Nur Gide; Camelia Quek; Peter Hersey; Wolfgang Weninger; Warwick J. Britton; Georgina V. Long; Richard A. Scolyer and Umairainthan Palendira

POSTER LOCATION: V2.2

ABSTRACT: "Therapeutic blockade of immune checkpoints has revolutionised cancer treatment. Despite durable objective responses in many cancer types, more than half of those treated develop resistance. Efforts to improve the efficacy of these treatments are confounded by the lack of understanding of the exact populations and phenotypes of immune cells that are critical in an anti-PD1 mediated response. Here we show that a subset of tumour-infiltrating CD8+ T cells are CD69+CD103+ tumour-resident CD8+ T cells. Importantly, the density of these cells correlated with a better overall survival than total CD8+ T cell counts in untreated stage III metastatic melanoma. Phenotypic characterization of tumour resident cells by flow cytometry showed that checkpoint expression of PD-1, TIM-3, and 2B4 was indeed largely confined to this subset of tumour-infiltrating T cells. In line with this, we also found this population to expand early during single agent anti-PD-1 therapy. In addition, here we also show that local IL-15 expression levels not only strongly correlate with patient survival, but also are likely to be critical for the differentiation of these tumour-resident CD8+ T cells. Our results suggest current immunotherapies with checkpoint inhibitors or IL-15 could potentially harness resident populations for their effectiveness. As such, CD103+ CD69+ CD8+ tumour resident cells might serve as a potential biomarker for the prediction of patient responsiveness to cancer intervention therapies"
ABSTRACT: Background: Communication triggered by receiving personal melanoma genomic risk may influence the social implications of this information. Delivering personal genomic risk information might also cause unnecessary harms (e.g. over-screening).

Aim: To identify predominant themes in conversations prompted by receiving personalised genomic risk of melanoma with family, friends and health professionals.

Methods: We used a mixed-methods approach. Participants without a personal history and unselected for a family history of melanoma (n=103, aged 21-69, 53% women) completed a questionnaire 3-months after receiving their personalised melanoma genomic risk. Semi-structured interviews were undertaken with 30 participants at high, average and low genomic risk. Data were analysed thematically.

Results: From questionnaires, 74% of participants communicated their genomic risk information with family, 49% with friends. Communication with a health professional differed by risk level: 41%, 16% and 12% for high, average and low risk, respectively (P=0.01). Qualitative analysis showed that perceived ‘shared risk’ and interest of family and friends were motivations for discussing risk information. Participants perceived family members to be supportive and interested in the information when sharing. Conversations were prompted with family and health professionals about sun protection and skin checks, and general conversations about melanoma risk with friends.

Conclusions: In our study, more participants at high risk communicated with health professionals, which suggests that it encouraged risk-appropriate screening. The largely positive and neutral interactions reported by participants suggest that delivering melanoma genomic risk to the public is acceptable, and may lead to improved disease risk perception and healthy behaviour change among family and friends.

“Describing the immune landscape across metastatic breast cancer lesions”

AUTHOR/S: Ghamdan Al-Eryani, Simon Junankar; Tri Phan; Alexander Swarbrick
POSTER LOCATION: H2.1
ABSTRACT: Cancer studies over the past decade have increasingly shown the importance of the immune system in malignancy, with growing evidence supporting the evaluation of tumour infiltrating leukocytes in in the prognosis and treatment of all cancer types. The significance of the immune system in cancer is however best epitomised by the success of phase III clinical trials using immune checkpoint inhibitors and their translation to routine use in the clinic for certain cancer types. Whilst still an ongoing effort, the achievements of currently approved immunotherapies appear to be relatively limited when extended to breast cancer. This emphasises how poorly we understand the dynamic cross-talk between cancer cells and the immune system throughout tumour progression and metastasis. Our lab has initiated a project where we will describe the immune landscape of metastatic breast cancer on a single-cell level using the 10x Chromium platform. We have successfully captured 8 clinical samples to date, providing us an unprecedented snapshot into these tumours intricate circuits crossing stromal, cancer and immune cells. Using this strategy, we aim to identify novel targets for immunotherapy with the hope of delivering long-term survival outcomes to metastatic breast cancer patients.

“Diagnostic and prognostic utility of Mastermind-like 2 (MAML2) gene rearrangement detected by fluorescent in-situ hybridization (FISH) in mucoepidermoid carcinoma.”

AUTHOR/S: Peter P Luk, Christina Selinger, James Wykes, Tim Eviston, Rafael Ekmejian, Jess Tay, Trina Lum, Sandra A O’Toole, Jonathan R Clark, and Ruta Gupta
POSTER LOCATION: H2.3
ABSTRACT: Aims: Mucoepidermoid carcinoma (MEC) is the most common salivary gland malignancy. A proportion of MECs have been shown to harbour MAML2 translocation. This study evaluates the diagnostic and prognostic utility of MAML2 in MEC.

Methods: Salivary gland malignancies at Royal Prince Alfred Hospital and Sydney Head and Neck Cancer Institute (1989-2014) were reviewed to identify MECs. Histopathologic evaluation, immunohistochemical and fluorescent in-situ hybridization (FISH) studies were performed. Additional 9 cases of morphologic mimics of MEC were also analysed for MAML2 rearrangement. Clinical follow-up was obtained.

Results: 40 cases of MEC were identified. Parotid gland was most common site (73%). The age range was 15 to 79 years (mean: 47 years). The tumour size ranged from 4-70mm (mean: 22mm). 37 cases were suitable for FISH and 31 (84%) cases were positive for MAML2 translocation, including oncocytic and clear cell variants of MEC. The 9 morphologic mimics of MEC did not show MAML2 rearrangement. MAML2 translocation did not correlate with histologic grade, stage,
nodal metastases, recurrence or survival, limiting its prognostic utility. **Conclusion:** FISH for MAML2 rearrangement has high sensitivity and specificity for MEC. Thus it is a useful diagnostic tool, particularly in cases with limited material or variant morphology.

**“Diagnostic and prognostic utility of MYB gene rearrangement detected by fluorescent in-situ hybridization (FISH) in adenoid cystic carcinoma.”**

**AUTHOR/S:** Peter P Luk, Christina I Selinger, Timothy J Eviston, Rafael Ekmejian, Denise Foo, Jessica Tay, Kan Gao, Sydney Ch’ng, Sandra A O’Toole, Jonathan R Clark, Ruta Guptaa

**POSTER LOCATION:** H3.1

**ABSTRACT:** **Objectives:** MYB rearrangement has been described in a proportion of adenoid cystic carcinoma (ACC). This study evaluates the diagnostic and prognostic utility of MYB rearrangement in ACC.

**Materials and Methods:** Salivary gland malignancies at the Sydney Head and Neck Cancer Institute (1989-2014) were reviewed. Histopathologic evaluation, and fluorescent in-situ hybridization (FISH) studies were performed on ACCs and their morphologic mimics. Clinical follow-up was obtained.

**Results:** 39 cases of ACC were identified with approximately 50% arising within the parotid gland. The age range was 19 to 80 years (median: 45 years). The tumor size ranged from 9-44mm (mean: 22mm). 3 locoregional recurrences, 7 distant metastases and 8 ACC related deaths were seen over a 22-year follow-up period. Nodal metastases were the most significant predictor of disease specific survival (p=0.019). 34 cases were suitable for FISH and 16 (47%) cases showed MYB rearrangement. MYB rearrangement was not seen in any cases of polymorphous low grade adenocarcinoma or epithelial myoepithelial carcinoma. MYB rearrangement was not seen in any of the high grade ACC or those with high grade transformation. MYB rearrangement was seen in 5 (50%) patients with recurrence/metastases and in 11 (45%) of those without.

**Conclusion:** FISH for MYB rearrangement has high specificity but low sensitivity for ACC. MYB rearrangement did provide prognostic information in this cohort.

**“Experimental liver cancer treated with DPP4 inhibition, metformin, or anti-PD1.”**

**AUTHOR/S:** Mark Gorrell, Natasa Polak; Stephanie Wetzel; James M. Henderson; James G. Kench; Geoffrey W. McCaughan

**POSTER LOCATION:** H7.2

**ABSTRACT:** **Background:** Hepatocellular carcinoma (HCC) is a primary liver malignancy that generally develops from chronic liver scarring. Sorafenib is a kinase inhibitor that is in clinical use to treat HCC. 1G244 is an immunostimulator that inhibits dipeptidyl peptidease 8 (DPP-8) and DPP-9. Anti-PD1 is an immune checkpoint inhibitor used to treat melanoma and lung cancer but untested in liver cancer. The antidiabetic drugs Sitagliptin and Metformin exhibit anti-tumour effects via DPP4 inhibition and AMPK activation, respectively.

**Aim:** To use a novel mouse model of HCC to investigate various agents in primary liver cancer.

**Methods:** Liver from 24-week-old male mice was analysed following HCC induction using diethyl nitrosamine (DEN), high fat diet (HFD) and the hepatotoxin thioacetamide (TAA). Potentially therapeutic interventions were provided for the final 4 weeks. Lesions, encompassing small cell change, focal fatty change, dysplasia, HCC and necrosis, were counted on sections.

**Results:** All livers had HCC. Blood glucose levels, steatosis and fibrosis were elevated in all groups of mice. The total numbers of lesions in both Sorafenib and Sorafenib plus 1G244 treated mice were less than their controls. Sitagliptin plus Metformin in a prevention protocol significantly decreased the total number of liver lesions. Anti-PD1 treated mice had more dysplastic lesions than their controls. Number of dysplastic/tumour spots visible on the liver surface was similar between all groups. There were no significant differences in the number of HCC lesions in this 24-week timeframe.

**“Exploring Salivary Duct Carcinoma: Clinicopathologic Features, Morphologic Spectrum and Genetic Changes”**

**AUTHOR/S:** Peter P Luk, Jared Weston, Christina Selinger, Tim Eviston, Trina Lum, Sandra A O’Toole, Jonathan R Clark, and Ruta Guptaa
**ABSTRACT:** Background: Salivary duct carcinoma (SDCa) have been slow in gaining recognition. Awareness, high index of suspicion and clinicopathologic correlation are essential for accurate diagnosis. Genetic changes like HER2 amplification and BRAF mutation are being explored in SDCa.

**Methods:** Salivary gland malignancies at Royal Prince Alfred Hospital and Sydney Head and Neck Cancer Institute (1989-2014) were reviewed to identify SDCa.

**Results:** 22 cases of SDCa were identified predominantly in men, age range 41-88 years, predominantly involved the parotid with size range 15-90mm. Facial nerve deficit and cervical lymph node metastases were present in 21% and 71% patients respectively, requiring salivary gland resection with neck dissection. Histologically, the tumours resembled high-grade invasive and in-situ ductal carcinoma of breast. Micropapillary, rhabdoid and mucinous variants were seen. HER2 was positive in 48% and BRAF (V600E) mutation present in 27%. Most patients received adjuvant radio and chemotherapy. 10 patients died of disease within 6-33 months (median 13 months). 5 patients developed local recurrence. 10 patients developed lung, bone, liver, axilla, mediastinal and brain metastases.

**Conclusion:** SDCa are aggressive malignancies with a large histopathologic spectrum including micropapillary and sacromatoid variants. HER2 amplification, BRAF mutation detectable by ancillary diagnostic techniques may provide therapeutic options requiring accurate diagnosis.

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**“Fluorescent in situ Hybridisation: A Novel Approach to Salivary Gland Tumours.”**

**AUTHOR/S:** Christina Selinger, Peter Luk, Jared Weston, Jonathan R Clark, Sandra O’Toole, Ruta Gupta

**POSTER LOCATION:** H5.1

**ABSTRACT:** Background: Specific translocations have recently been described in salivary gland adenoid cystic carcinoma (AcCa), mucoepidermoid carcinoma (MEC), and hyalinising clear cell carcinoma (HCCCa), and Her2 amplification in most salivary duct carcinomas (SDCa).

The diagnostic sensitivity and specificity of rearrangements of MYB in AcCa and of MAML2 in MEC are under investigation with speculations about their prognostic implications.

**Aim:** To evaluate the diagnostic and prognostic utility of these genetic alterations.

**Methods:** Fluorescent in situ hybridisation (FISH) studies using ZytoLight SPEC MYB Break Apart Probe were performed on AcCa (n=10), ZytoLight SPEC MAML Break Apart Probe on MEC (n=10), PathVysion HER-2 DNA Probe on SDCa (n=4) and Vysis LSI EWSR1 Probe on HCCCa (n=1).

**Results:** AcCas (n=10) demonstrating a spectrum of histomorphologic and prognostic features including low grade (n=4), solid high grade (n=1), dedifferentiated AcCa (n=1), metastatic to lymph node (n=2), metastatic to bone (n=1) and tracheal AcCa (n=1) were selected. MYB rearrangement was seen in 3 (30%) of the cases including a case each of bone metastases and extensive infiltration of the underlying skull bone.

All the SDCas (n=4) demonstrated Her2 amplification and the HCCCa demonstrated EWSR1 rearrangement.

**Conclusions:** FISH studies augment the diagnostic and prognostic accuracy in the appropriate morphologic setting. Work was performed: Department of Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital, Sydney. Statement of Contribution: Original idea was contributed by Ruta Gupta and Sandra O’Toole, FISH analysis was performed by Christina Selinger, Ruta Gupta and Sandra O’Toole. Peter Luk, Jared Weston and Jonathan R Clark contributed to histopathological analysis.

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**“Full-Field Digital Mammography versus Screen-Film Mammography for Breast Cancer Screening”**

**AUTHOR/S:** Rachel Farber; Katy Bell; Kevin McGeechan; Alexandra Barratt

**POSTER LOCATION:** H1.1

**ABSTRACT:** Most breast screening programmes worldwide have replaced the use of screen-film mammography (SFM) with full-field digital mammography (FFDM) in expectation of technical, clinical and economic advantages. However, the effects of this practice shift on patient health outcomes in screening programmes is unclear. We designed a protocol for a systematic review to examine and compare the benefits and harms from the transition from film mammography to digital mammography by measuring the effect of this move on detection rates and interval cancer rates. This protocol will allow us to examine if with the change in technology there is a change in detection, and if that change is seen correspondingly in interval rates. We will also compare benefits and harms from changes in measurements of cancer stage, tumour size,
tumour grade, nodal status and mortality. This will allow us to assess if there is a change in the type of cancers being detected: cancers in which early treatment decreases interval rates and mortality rates (clinically important cancers) versus cancers where treatment has no benefit (overdiagnosed cancers). We will collate all published data of screening populations that report both benefits (e.g. lower interval cancer rate; breast cancer mortality reduction) and harms (e.g. false-positive rates; overdiagnosis). We will evaluate the extent to which any improved sensitivity with FFDM reflects the detection of clinically important cancers. These results are likely to have important implications for breast cancer screening practice and policy both in Australia and internationally.


AUTHOR/S: Nicole Rankin, Christopher Slatore, Emily Stone

POSTER LOCATION: H6.2

ABSTRACT: Aim: Lung cancer screening studies have begun to document potential and actual challenges in implementation after the US Preventive Services Task Force recommended screening in 2013. Screening studies are yet to fully grapple with the science of measuring implementation outcomes or determining how implementation ‘success’ can be replicated across settings.

Methods: We used an implementation science framework that proposes the key implementation outcomes as acceptability, adoption, appropriateness, feasibility, penetration, costs and sustainability. We conducted a Medline search using keyword ‘lung neoplasms’, ‘mass screening’ (MESH terms) and ‘implementation’ (keyword search). Inclusion criteria were English language publications within a ten year period (2007-2016) to examine whether lung cancer screening publications have addressed these implementation outcomes.

Results: We retrieved 68 publications, 16 were excluded and 5 of 52 studies (screening program evaluations) specifically addressed implementation issues. Cost (or insurance coverage) was addressed in each study and most of evidence reviews (n=17). Acceptability, adoption, feasibility, fidelity and appropriateness outcomes were addressed infrequently, while penetration and sustainability outcomes were not addressed at all. One policy statement focused specifically on implementation outcomes. Surveys of health care providers and patients focused on service outcomes, acceptability and feasibility.

Conclusion: This literature review highlights that initial work in to implement lung cancer screening programs has primarily focused on issues about cost. As questions about screening move beyond efficacy and effectiveness, there is significant potential to use implementation science frameworks to consider how screening programs are delivered, to determine outcomes of significance and how these are best measured.

“Mammary Analogue Secretory Carcinoma: An Evaluation of its Genetic and Clinical Characteristics”

AUTHOR/S: Peter P Luk, Christina Selinger, Tim Eviston, Trina Lum, Sandra A O’Toole, Jonathan R Clark, Ruta Gupta

POSTER LOCATION: H3.2

ABSTRACT: Aims: Mammary analogue secretory carcinoma (MASC) is a recently described salivary gland malignancy. This study evaluates the characteristics and long-term clinical behaviour of MASCs.

Methods: Salivary gland malignancies at Royal Prince Alfred Hospital and Sydney Head and Neck Cancer Institute (1989-2014) were reviewed to identify MASCs. Histopathologic evaluation, immunohistochemical and fluorescent in-situ hybridization (FISH) studies were performed.

Results: Ten cases of MASC were identified with age range 19-82 years (mean: 41 years). The tumour size ranged from 14-50mm (mean: 22mm) and commonly involved the parotid. MASCs predominantly showed a cystic pattern with thin, pale eosinophilic secretions and monotonous cells with vacuolated eosinophilic cytoplasm and a small nucleus with a small distinctive nucleolus. The tumours were positive with S100, MUC4, CK7, GCDFP-15 and negative for p63, CK5/6 and calponin. FISH showed ETV6 rearrangement in all tested cases with one case showing a novel rearrangement pattern. One case showed lymph node involvement. Local failure was seen in one patient.

Conclusion: MASCs have relatively specific histopathologic features and immunohistochemical profile that distinguish them from their mimics. FISH plays a confirmatory role. An indolent long-term clinical course was observed despite involvement of intraparotid lymph node and microscopically involved/close margins in 70% cases.
“MCL-1 inhibition provides a new way to suppress breast cancer metastasis and increase sensitivity to dasatinib”

AUTHOR/S: Samantha Richelle Oakes, Adelaide I. J. Young; Andrew M. K. Law; Lesley Castillo; Sabrina Chong; Hayley D. Cullen; Martin Koehler; Sebastian Herzog; Tilman Brummer; Erina F. Lee; Walter D. Fairlie; Morghan C. Lucas; David Herrmann; Amr Allam; Paul Timpson; D. Neil Watkins; Ewan K. A. Millar; Sandra A. O'Toole; David Gallego-Ortega

POSTER LOCATION: H6.1

ABSTRACT: Background: Metastatic disease is largely resistant to therapy and accounts for almost all cancer deaths. Myeloid cell leukemia-1 (MCL-1) is an important regulator of cell survival and chemo-resistance in a wide range of malignancies, and thus its inhibition may prove to be therapeutically useful.

Aim: To examine whether targeting MCL-1 may provide an effective treatment for breast cancer

Methods: We constructed inducible models of BIMs2A expression (a specific MCL-1 inhibitor) in MDA-MB-468 (MDA-MB-468-2A) and MDA-MB-231 (MDA-MB-231-2A) cells.

Results: MCL-1 inhibition caused apoptosis of basal-like MDA-MB-468-2A cells grown as monolayers, and sensitized them to the BCL-2/BCL-XL inhibitor ABT-263, demonstrating that MCL-1 regulated cell survival. In MDA-MB-231-2A cells, grown in an organotypic model, induction of BIMs2A produced an almost complete suppression of invasion. Apoptosis was induced in such a small proportion of these cells that it could not account for the large decrease in invasion, suggesting that MCL-1 was operating via a previously undetected mechanism. MCL-1 antagonism also suppressed local invasion and distant metastasis to the lung in mouse mammary intraductal xenografts. Kinomic profiling revealed that MCL-1 antagonism modulated Src family kinases and their targets, which suggested that MCL-1 might act as an upstream modulator of invasion via this pathway. Inhibition of MCL-1 in combination with dasatinib suppressed invasion in 3D models of invasion and inhibited the establishment of tumors in vivo.

Conclusion: These data provide the first evidence that MCL-1 drives breast cancer cell invasion and suggests that MCL-1 antagonists could be used alone or in combination with drugs targeting Src kinases such as dasatinib to suppress metastasis.

“Multiparametric prostate MRI. Why are we driving Fred Flintstone’s car?”

AUTHOR/S: Roger Bourne, Eleftheria Panagiotaki, Daniel Alexander, Gregory Karczmar, Aytekin Oto

POSTER LOCATION: V3.1

ABSTRACT: Background: Detection of significant prostate cancer is enhanced when biopsy is guided by multiparametric MRI (mpMRI). The DWI (diffusion) component of the mpMRI scan has stronger correlations with both cancer grade and volume than T2 and DCE (dynamic contrast), and there is growing evidence that the DCE component may be redundant. Although DWI is more accurate than T2 and DCE for cancer detection, at present it is performed in a very primitive way – by calculating an apparent diffusion coefficient (ADC). The ADC is a crude single number summary of a complex and potentially information-rich signal.

Aim: To increase the sensitivity and specificity of prostate mpMRI by exploiting the tissue structure dependence of DWI.

Methods: New methods of diffusion acquisition include multiple echo times and diffusion times and ‘deconstruct’ the simplistic approaches based on b-factors alone. Novel biomarkers are validated against whole mount histopathology of radical prostatectomy specimens.

Results: Advanced scanning and data analysis methods enable the replacement of naive ADC analysis with compartment models based on tissue microstructure. These strategies enable non-invasive generation of biomarkers that correspond directly with histological cancer markers including gland differentiation and tumour cell density.

Conclusions: Pilot studies suggest advanced diffusion techniques for prostate cancer characterization will provide increased sensitivity and specificity over ADC and can be performed in clinically feasible scan times.

“Novel targets for an in vivo dendritic cell anti-prostate cancer vaccine”

AUTHOR/S: Sutherland, S, Fromm, P, Barnard, R, Horvath, L, Mahon, K, Clark, G and Hart, D.

POSTER LOCATION: V4.1
“p16 expression in cutaneous squamous cell carcinoma of the head and neck is not associated with integration of high risk HPV DNA or prognosis”

AUTHOR/S: Satgunaseelan L, Chia N, Suh H, Virk S, Ashford B, Lum T, Ranson M, Clark J, Gupta R.
POSTER LOCATION: H4.3
ABSTRACT: Head and neck cutaneous squamous cell carcinoma (HNCSCC) can present with cervical metastases without an obvious primary. Immunohistochemistry for p16 is established as a surrogate marker of human papillomavirus (HPV) in oropharyngeal cancer. p16 expression in HNCSCC needs to be elucidated to determine its utility in predicting the primary site. The aim of this study was to evaluate the rate of p16 expression in HNCSCC and its association with prognostic factors and survival. p16 immunohistochemistry was performed on 166 patients with high risk HNCSCC (2000-2013) following histopathology review. Chromogenic in situ hybridisation (CISH) for HPV was performed. Fifty-three (31.9%) cases showed strong, diffuse nuclear and cytoplasmic p16 expression including 14 (41%) non-metastatic and 39 (29.5%) metastatic tumours (p=0.21). HPV CISH was negative in all cases. p16 expression significantly increased with poorer differentiation (p=0.033), but was not associated with size (p=0.30), depth of invasion (p=0.94), lymphovascular invasion (p=0.31), perineural invasion (p=0.69), keratinisation (p=0.99), number of involved nodes (p=0.64), extranodal extension (p=0.59) or survival. Nearly 32% of HNCSCCs, particularly poorly differentiated HNCSCCs, show p16 expression. A primary HNCSCC should be considered in p16 positive neck node metastases in regions with high prevalence of HNCSCC. p16 expression is not associated with improved survival in HNCSCC. (published - Pathology. 2017 Jun 26. pii: S0031-3025(17)30068-5. doi: 10.1016/j.pathol.2017.04.002. [Epub ahead of print])

“Precision medicine for prostate cancer: what are we missing in our genomic data?”

AUTHOR/S: Prof. Vanessa M. Hayes, Weerachai Jaratlerdsiri, Desiree C. Petersen, Riana Bornman, Christopher M. Hovens, Eva K.F. Chan
POSTER LOCATION: H8.1
ABSTRACT: Background: Prostate cancer is a genetic disease. Presenting with a high degree of clinical and genetic heterogeneity, prostate cancer is an ideal candidate for the hopes of precision medicine. Unlike other cancers, however, prostate cancer acquires a disproportionate number of large complex genomic rearrangements during tumourigenesis. Problem: It is well established that detecting the full range of large structural genomic variants is challenging using bioinformatics interrogation of clinically applicable short-read next generation sequencing (NGS). Aim: The aim of this study was to use a new clinically cost-effective non-sequencing technology to capture a near to complete spectrum of large structural variations impacting prostate carcinogenesis. Methods: We adapted the nanochannel optical mapping technology from Bionano Genomics to generate the first complete human genome maps from both normal and tumour-normal primary and metastatic prostate cancer pairs. Results: As next generation mapping (NGM) allows for the interrogation of megabase length DNA molecules outside the detection range of single-base resolution NGS, we were able to use this technology to capture a ‘birds-eye’ view of the prostate cancer genome. Specifically, by applying NGM to prostate cancer we identify: (i) a novel spectrum of large genomic rearrangements undetectable using NGS, (ii) an over-representation of large insertion or duplication events, (iii) advantages of direct tumour-normal comparative analyses via de novo assembly and (iv) hidden information within NGS data that becomes apparent with NGM-guided orientation. Conclusion: We use a new technology to identify novel oncogenic drivers and potentially actionable therapeutic targets of relevance to prostate cancer.

“Pre-operative exercise in patients with cancer: a systematic review with meta-analysis”

AUTHOR/S: Daniel Steffens; Paula Beckenkamp; Mark Hancock; Michael Solomon; Jane Young
POSTER LOCATION: V3.2
ABSTRACT: Aim: To investigate the effectiveness of pre-operative exercises in patients undergoing oncological surgery, on post-operative complications, length of hospital stay and quality of life. Design: Systematic review with meta-analysis. Methods: Randomised controlled trials investigating the effectiveness of pre-operative exercise (compared to no intervention, placebo or minimal intervention) for patients undergoing oncological surgery were searched using electronic databases and grey literature from inception to November 2016. Outcomes included post-operative complications, length of hospital stay and quality of life. Methodological quality was assessed using the Cochrane ‘Risk of Bias’ tool and quality of evidence was assessed using the GRADE approach. Meta-
analysis was performed using random-effects model.

**Results:** Seventeen studies (reporting 6 forms of malignancies) involving 810 participants were included. There is moderate quality of evidence that pre-operative exercise, compared to control, significantly reduced cardiopulmonary complication (relative risk: 0.65, 95% confidence interval [CI]: 0.49 to 0.87) and length of hospital stay (mean difference [MD]: -2.86, 95%CI: -5.40 to -0.33) in patients undergoing lung resection. Pre-operative exercise was not effective in reducing length of hospital stay (MD: 2.00, 95%CI: -2.35 to 6.35) in patients with oesophageal cancer. Only individual studies reported quality of life, therefore a meta-analysis for this outcome was not possible.

**Conclusions:** There is moderate-quality evidence that pre-operative exercise is effective in reducing post-operative complications and length of hospital stay in lung cancer patients. The evidence that pre-operative exercise reduces complications, length of hospital stay and improves quality of life in other groups of patients undergoing oncological surgery remains inconclusive.

“Radiotherapy and Her2 targeting agents: is there a positive therapeutic interaction?”

**AUTHOR/S:** N Suchowerska, Ana Dos Santos Esteves, S Carroll, JM Toohey, J G Lyons, A/Prof J Beith, L J Rogers, Shirley Baxter, D R McKenzie

**POSTER LOCATION:** V2.1

**ABSTRACT:** Fifteen percent of breast cancers over-express the Her2 receptor. Treatments targeting this receptor, such as trastuzumab, pertuzumab and T-DM1 have led to significant improvement in survival of these previously high risk cancers. Further improvement has been shown with combining these agents. There is a paucity of information on the interaction of single or combination HER2 targeted therapy with concurrent radiation. Our aim is to identify interactions between Her2+ targeting agents and ionising radiation. Two molecular subtypes of HER2+ breast cancer (HCC-1954 and BT-474) were treated with Her2 targeting agents and radiation, individually and in combination. The alpha/beta ratio as a measure of radiosensitivity was experimentally determined. Synergy($S$) is defined as the fractional difference between observed($S_o$) and predicted survival for each treatment given alone($S_1$ × $S_2$):

$$S = \frac{S_o - S_1 \times S_2}{S_o}$$

The alpha/beta ratio for HCC-1954 (ER-/PR-/Her2+) and BT474 (ER-/PR+/Her2+) are 35Gy and 5Gy respectively, highlighting heterogeneous treatment responses. Trastuzumab or Pertuzumab alone had no effect on the survival of HCC-1954, but when combined with radiation, a synergistic interaction was observed. T-DM1 alone had a significant effect on survival of HCC-1954 and the combination of T-DM1 with radiation showed strong synergy with a 60% survival decrease relative to T-DM1 alone. Trastuzumab alone caused 50% decrease in survival of BT-474, but when combined with radiation did not yield further decrease in survival, indicating no therapeutic advantage.

Our results stress the importance of determining treatment interactions [radiation therapy with drugs or agents] prior to starting clinical trials. The assumption that a combination of treatments will result in an improved therapeutic response is clearly not always true.

**Acknowledgements**

We acknowledge funding from the Sydney Breast Cancer Foundation

“Re-instating the therapeutic efficacy of doxorubicin using a novel combination therapy that utilizes lysosomal permeabilisation with Dp44mT or DpC”

**AUTHOR/S:** Nicole A. Seebacher, Alexandra E. Stacy, Des R. Richardson, and Patric J. Jansson

**POSTER LOCATION:** H5.2

**ABSTRACT:** Aims: This study investigated the mechanisms by which the anti-cancer agent, di-2-pyrdylketone 4,4-dimethyl-3-thiosemicarbazone (Dp44mT) and the clinically trialled, di-2-pyrdylketone 4-cyclohexyl-4-methyl-3-thiosemicarbazone (DpC), re-instate doxorubicin (DOX) efficacy, in P-glycoprotein (Pgp) expressing, drug-resistant cells.

**Methods:** All cell lines were assessed for Pgp protein expression and function using Western Blotting and Rhodamine 123 retention assays. Drug Cytotoxicity was measured with MTT assays and drug synergy calculated using the Chou-Talalay method. Drug cellular localisation was visualised using fluorescence microscopy.

**Results:** These studies demonstrated that both Dp44mT and DpC are transported into lysosomes via Pgp transport activity, where they induce lysosomal-membrane permeabilisation to release DOX trapped within lysosomes. This novel strategy of loading lysosomes with DOX, followed by permeabilisation with Dp44mT or DpC, results in the relocalisation of stored DOX from its lysosomal ‘safe house’ to its nuclear targets, markedly enhancing cellular toxicity against resistant tumour cells. The combination of Dp44mT or DpC with DOX showed a very high level of synergism in multiple Pgp-expressing cell types, including cervical and breast (CI: 0.13 ± 0.08 – 0.76 ± 0.10) cancer cells. These studies revealed that
the level of drug synergy was proportional to Pgp activity. Interestingly, synergism was ablated by inhibiting Pgp using the inhibitor, Elacridar, or by silencing Pgp (CI: 0.78 ± 0.10 - 0.91 ± 0.14), demonstrating the importance of Pgp in the synergistic drug interaction. Furthermore, lysosomal-membrane stabilization inhibited the relocalisation of DOX from lysosomes to the nucleus upon combination with Dp44mT or DpC (CI: 0.98 ± 0.07 - 1.08 ± 0.09), preventing synergism. This latter observation demonstrated the importance of lysosomal-membrane permeabilisation to the synergistic interaction between these agents.

**Conclusions:** The synergistic and potent anti-tumour efficacy observed between DOX and thiosemicarbazones represents a promising treatment combination for advanced cancers, which are heterogeneous and composed of non-Pgp- and Pgp-expressing tumour cells.

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**“Serum exosomes in glioblastoma patients: an opportunity for non-invasive diagnosis and monitoring.”**

**AUTHOR/S:** Michael Buckland, Kimberley Kaufman; Saeideh Ebrahimkhani; Susannah Hallal; Brindha Shivalingam

**POSTER LOCATION:** H4.1

**ABSTRACT:** Surrogate endpoints are increasingly important in clinical trials, enabling faster regulatory approvals for therapeutics in diseases with poor outcome, and assisting in the new generation of adaptive clinical trial design. Exosomes are nano-sized extracellular vesicles shed by cells of all types, and their release is upregulated in pathological conditions. Exosomes can traverse the blood-brain barrier, and brain tumour exosomes have previously been found in the blood. Exosomes encapsulate a molecular cargo that is typical of their cell of origin. The promise of exosomal miRNA as a GBM biomarker has recently been demonstrated in two studies that have reported changes in serum EV miRNA composition in GBM patient sera. However these studies examined only a small number of patients at only handful of miRNA. With emerging technology it is now feasible to perform an unbiased assessment of all exosomal miRNA from any cell type. We have successfully optimised serum exosome purification and RNA isolation protocols, as well as unbiased deep sequencing and downstream bioinformatics analysis in our pilot study of eight GBM patients and matched controls. This has identified numerous (>30) serum exosomal miRNAs with significant differential expression between controls and GBM. We are now analysing selected samples from the VERTU GBM clinical trial, with the hope of identifying an exosomal miRNA signature of GBM disease activity. This may be a valuable surrogate endpoint marker for future clinical trials, as well as assisting in future clinical management of patients with GBM.

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**“Somatic Mutations in Salivary Duct Carcinoma and Potential Therapeutic Targets”**

**AUTHOR/S:** Timothy Khoo, Bing Yu, Joel Smith, Angus Clarke, Peter Luk, Christina Selinger, Kate Mahon, Spiridoula Kraitsek, Carsten Palme, Michael Boyer, Marcel Dinger, Mark Cowley, Sandra O’Toole, Jonathan Clark, Ruta Gupta

**POSTER LOCATION:** H3.3

**ABSTRACT:** Background: Salivary duct carcinomas (SDCa) are rare highly aggressive malignancies. Most patients die from distant metastatic disease within three years of diagnosis. There are limited therapeutic options for disseminated disease.

**Methods:** Somatic mutation analysis was performed on DNA extracted from 15 archival cases of SDCa using the targeted Illumina TruSeq Amplicon Cancer Panel. Potential targetable genetic alterations were identified using extensive literature and international somatic mutation database (COSMIC, KEGG) search. Immunohistochemistry for androgen receptor and immunohistochemistry and fluorescent in situ hybridization for HER2 were also performed.

**Results:** 11 cases showed androgen receptor expression and 5 cases showed HER2 amplification. Somatic mutations with additional available targeted therapies were identified in 6 patients: EGFR (p.G721A: Gefitinib), PDGFRA (p.H845Y: Imatinib and Crenolanib), PIK3CA (p.H1047R: Everolimus), ERBB2 (p.V842I: Lapatinib), HRAS (p.Q61R: Selumetinib) and KIT (p.T670I: Sorafenib). Furthermore, alterations in PTEN, PIK3CA and HRAS that alter response to androgen deprivation therapy and HER2 inhibition were also seen.

**Conclusion:** SDCa show multiple somatic mutations, some that are amenable to pharmacologic manipulation and others that confer resistance to treatments currently under investigation. These findings emphasize the need to develop testing and treatment strategies for SDCa. Work was done at the Central Clinical School, The University of Sydney, Sydney, Australia. Statement of Originality: I contributed the bulk of the somatic mutation analysis from the data produced from the TruSeq Amplicon Cancer Panel.
Further, I conducted the initial investigation identifying the specific mutations for which targeted therapies would be applicable.

“Systematic screening reveals candidate miRNAs for treatment of high-risk neuroblastoma”

**AUTHOR/S:** Eoin Dodson, Iva Nikolic, Benjamin Elsworth, Daniel Thomas, Kate Gould, Glenn Marshall, Kaylene Simpson, Alexander Swarbrick  
**POSTER LOCATION:** V4.2  
**ABSTRACT:** Neuroblastoma (NB) is a cancer found in children aged 0-5. NB accounts for 6% of childhood cancer diagnoses, but ~15% of childhood cancer deaths. MYCN oncogene amplification confers very poor outcomes. No targeted therapies are available and toxic high-dose chemotherapy remains the core treatment option for patients with NB. MicroRNAs (miRNAs) are a class of non-coding RNAs which repress the expression of mRNA target genes. A handful of miRNAs have already been associated with NB, although a comprehensive and systematic analysis has not been performed. Only in recent years have miRNAs entered early-stage clinical trials (none in neuroblastoma). We performed a genome-wide screen of 1280 miRNAs in two NB cell lines (including MYCN-amplified Kelly cells). This screen was also performed in the presence of low dose chemotherapy. This allowed us to discover synthetic lethal miRNAs which synergize with chemotherapy, in addition to outright lethal miRNAs. We have validated the majority of these in additional cell lines. We have developed a novel bioinformatics tool to help us identify the direct target genes of these miRNAs. Clinical relevance of miRNAs and their targets is being examined using cohorts of NB tumours with known outcomes. In order to assess the miRNAs in vivo as potential therapeutics we aim to use nanoparticle delivery vectors in patient-derived xenograft models of high-risk NB.

“Targeting the Src/JAK/STAT3 signalling pathway: A novel and promising therapeutic strategy for pancreatic cancer”

**POSTER LOCATION:** V1.1  
**ABSTRACT:** Introduction: Pancreatic cancer (PC) has a 5-year survival of only 6%, and persists as the 4th most common cause of cancer–related death in Western societies. A more tailored treatment approach may be beneficial as the current standard–of–care therapies offer only a modest increase in overall patient survival. Recent large–scale genomic studies have revealed that the Src/JAK/STAT3 signalling pathway is deregulated in up to 35% of PC, and is yet to be systematically examined in this disease. Consequently, we hypothesized that targeting pancreatic tumours with activated JAK/STAT3 signalling with selective JAK1/JAK2 or JAK3 inhibitors and an Src inhibitor represents a promising novel therapeutic strategy for this disease.  
**Materials and methods:** We utilized well–annotated patient–derived cell–line models (ICGC), along with cell–lines generated from the aggressive KPC mouse model. Using these pre–clinical models we assessed the in vitro efficacy of therapeutic strategies involving Src/JAK/STAT3 inhibition, using cell proliferation assays, 2D–drug synergy screens, and 3D organotypic invasion assays. Extracellular matrix integrity post–treatment was assessed using second– harmonic generation (SHG) imaging and picrosirius staining. We also used the syngeneic, orthotopic KPC mouse model to examine effects on immune–cell infiltrate.  
**Results:** We show that selected JAK and Src–inhibitors inhibit cell proliferation in candidate PDCLs and KPC lines, characterized by activated Src/JAK/STAT3 signalling, with combination therapy being synergistic in the majority of these cell–lines. Cell invasion was significantly inhibited in organotypic matrices, and there was decreased collagen contractility, and reduced fibrillar collagen coverage. We also show that these therapies reduce regulatory T–cells, MDSCs and tumour–associated macrophages.  
**Conclusion:** Our findings demonstrate the potential for tailored therapeutic strategies involving Src/JAK/STAT3 inhibition in PC, and suggest that therapeutic efficacy may be the result of targeting both tumour cells and the tumour microenvironment, as well as by overcoming tumour–induced immunosuppression.

“The Link Between Obstructive Sleep Apnea and Cancer: Hypoxia”

**AUTHOR/S:** Kristina M Cook  
**POSTER LOCATION:** H3.4
ABSTRACT: Obstructive sleep apnoea (OSA) affects 5% of the population and recent epidemiological studies have shown it is associated with cancer development and increased cancer mortality, though how this occurs at a fundamental level is unknown. OSA is characterised by episodic upper airway obstruction resulting in intermittent hypoxia and a decrease in blood oxygen levels.

Hypoxia inducible factor (HIF) is a transcription factor activated by low oxygen levels that can influence cancer growth and metabolism, and is associated with treatment resistance. In OSA, both HIF and NF-κB transcriptional activity is proposed to increase in affected tissues and this may include tumours in the body. However, we have yet to understand how HIF or NF-κB may be activated during rapid oxygen fluctuations, as compared to chronic tumour hypoxia, and how this may lead to altered cancer outcomes.

A model to study the effect of rapid, intermittent cycling oxygen levels, such as that seen in OSA, is needed to study the changes in gene expression and cell signalling induced by this novel form of hypoxia. Using information derived from real sleep data, a sleep apnoea bioreactor has been designed that accurately models physiological blood and tissue oxygen levels recorded during OSA. The bioreactor has been used to examine the effect of rapid, intermittent cycles of hypoxia in a series of glioblastoma cell lines.

“Uniting intuition and theory: enhancing the replicability of behaviour change interventions in cancer genetics”

AUTHOR/S: Natalie Taylor, Emma Healey, Sian Greening, Claire E Wakefield, Linda Warwick, Rachel Williams, Kathy Tucker
POSTER LOCATION: H1.4
ABSTRACT: Introduction: Despite considerable encouragement for healthcare professionals to use or be clear about the theory used in their improvement programmes, the uptake of these approaches to design interventions or report their content is lacking. Recommendations suggest healthcare practitioners work with social and/or behavioural scientists to gain expertise in programme theory, ideally before, but even during or after the work is done. We aim to demonstrate the extent to which an intuitive intervention designed by healthcare professionals to overcome patient barriers to communicating genetic cancer risk information to family members aligns with a theoretical framework of behaviour change.

Methods: As part of a quality improvement study, a team of genetic counsellors aimed to understand, and design interventions to overcome, the major barriers a group of familial cancer patients face around communicating hereditary cancer risk information to their relatives. A behavioural change specialist worked with the team to review and recode barriers and interventions according to the Theoretical Domains Framework (TDF) and 93 Behaviour Change Techniques (BCTs).

Results: Five themes emerged from the genetic counsellor coded barriers, which when recoded according to the TDF, represented seven domains of behaviour change. 45 experiential and intuitive interventions were used to tackle key barriers. These were represented by 24 BCTs, which were found to be used on 122 occasions. The full mapping exercise is presented.

Conclusion: Although the ideal is to use theory prospectively, or even whilst a project is underway, perhaps a more realistic starting point is to demonstrate to healthcare professionals how their intuition aligns with theory. Such an approach may highlight the additional benefits that theory has to offer and serve to promote its use in improvement.

“Using the epigenome to understand and better classify phyllodes tumours”

AUTHOR/S: Sandra O’Toole; Ruth Pidsley; Kate Harvey; Rooshdiya Karim; C.Soon Lee; Belinda Chan; Clare Stirzaker.
POSTER LOCATION: H1.2
ABSTRACT: Background: Phyllodes tumours are rare, comprising <1% of breast tumours. Their biology is poorly understood and they exhibit varying potential for recurrence and aggressive behaviour. It can be difficult to reproducibly split tumours into benign, borderline or malignant as no specific biomarkers currently exist to classify these tumours. Biomarkers that could accurately classify these lesions would be important in determining the most appropriate treatment, avoiding over or undertreatment.

A recently published study revealed that SETD2 and/or KMT2D (which encode histone methyltransferases involved in epigenetic regulation) were recurrently mutated in phyllodes tumours with 35% showing loss-of-function mutations. We hypothesised that different subtypes of fibroepithelial breast tumours show distinctive DNA methylation patterns with the aim of identifying potential clinical biomarkers to better diagnose and stratify these tumours.
Methods: We performed genome-wide DNA methylation profiling using the new Illumina MethylationEPIC BeadChip arrays on a cohort of 32 FFPE fibroepithelial tumours including fibroadenomas, benign, borderline and malignant phyllodes tumours.

Results: We found significant differences in DNA methylation between borderline and malignant PTs in particular. Analysis of this data has shown that the differentially methylated regions (DMRs) include genes that are involved in regulation of developmental pathways and cell fate (TBX5, HAND2, HOXC8, TWIST1, EN1) as well as cell migration (NRN1, NINJ2) and matrix remodelling (MXRA5, LTBP4).

Conclusions: These data constitutes the first assessment of genome-wide DNA methylation in these rare tumour types and offers a unique opportunity to identify biomarkers to better classify phyllodes tumours with strong potential for translation into practice.

“Working with clinicians to identify barriers to Family Cancer Clinic referrals for patients at high risk of Lynch syndrome”

AUTHOR/S: Rachel Williams, Janet C. Long; Deborah Debono; Melvin Chin; Natalie Taylor.

POSTER LOCATION: H4.2

ABSTRACT: Background: Referral rates to Family Cancer Clinics (FCC) for patients at high risk of Lynch syndrome are low. This study examined barriers to referral for colorectal cancer patients with mismatch repair deficiency identified through immunohistochemistry, at two large, Australian hospitals.

Methods: We used the Theoretical Domains Framework Implementation (TDFI) approach, a validated six-step process for changing clinical practice based on behaviour change theory. We established two multidisciplinary implementation teams (n=8 at Hospital A, n=11 at Hospital B) to process map current practice. A12-month retrospective audit showed referral rates of 36% and 13% at Hospital A and B respectively.

We report on referral rates (audit) and barriers to referral drawn from a number of different sources: (1) Minutes from four Implementation Team meetings; (2) the validated Influences of Patient Safety Behaviour Questionnaire (IPSBQ) (n=71); and (3) multidisciplinary focus groups and interviews (n=19).

Results: Baseline audits indicated only 24% of patients were appropriately referred. Barriers were identified in the domains of ‘environmental context and resources’ (problems finding referral forms, inability to track referrals, and suboptimal timing of pathology reports for follow up), ‘cognitive processes, memory and decision making’ (confusing terminology on pathology reports; lack of a structured process in case conferences) and ‘skills’.

Discussion: Input from all stakeholders: pathologists, surgeons, oncologists and genetic cancer services and triangulated data collection enabled a comprehensive approach to the problem of low referral rates. Understanding how psychosocial and environmental barriers impede behaviour change aids co-design of strategies to address them using matched behaviour change techniques.
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