# Lonsurf®

*trifluridine/tipiracil*

# *Evidence based* treatment option for pretreated mCRC* AND mGC** patients with ECOG/WHO 0-1[1-5]

*Adults with metastatic colorectal cancer previously treated with, or not candidates for fluoropyrimidine-, oxaliplatin-, & irinotecan-based chemotherapies, anti-VEGF agents and anti-EGFR agents.[3]

**Adults with metastatic gastric (mGC) or gastroesophageal junction adenocarcinoma previously treated with fluoropyrimidine-, platinum-, taxane- or irinotecan-based chemotherapy and if appropriate HER2/neu-targeted therapy.[3]

**PBS Information:** Authority required for the treatment of mCRC. Initial treatment of mCRC (STREAMLINED 8195).
For continuing treatment of mCRC (STREAMLINED 8183).
This product is not listed on the PBS for the treatment of mGC.

Please review Product Information before prescribing. To access a copy of the Product Information please go to www.servier.com.au/PI or telephone 1800 153 590.

**MINIMUM PRODUCT INFORMATION**

**LONSURF® 15/6.14mg, 20/8.19mg (trifluridine/ tipiracil hydrochloride)**. Contains lactose. **Therapeutic Indications:** Adult patients with metastatic colorectal cancer, previously treated with, or not candidates for fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents. Adult patients with metastatic gastric or gastroesophageal junction adenocarcinoma previously treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy. **Dose and Method of Administration:** Recommended starting dose of 35 mg/m2/dose taken orally twice daily on Days 1 to 5 and Days 8 to 12 of each 28-day cycle, within 1 hour after completion of the morning and evening meals. Do not exceed 80 mg/dose. Dose interruption, resumption and reduction details consult Approved PI. 3 dose reductions permitted to a minimum dose of 20 mg/m2 twice daily, dose escalation not permitted after a dose reduction. **Contraindications:** History of hypersensitivity to tipiracil, trifluridine or excipients. **Special Warnings and Precautions for Use:** ECOG ≥2. Bone marrow suppression: Complete blood cell counts (FBC) must be obtained prior to initiation. Consider repeat FBC on day 15 of cycle 1. For subsequent cycles obtain FBC prior to each cycle and more frequently as clinically indicated. Treatment must not be started if absolute neutrophil count <1.5 x 109/L, platelet count <75 x109/L, or unresolved Grade 3 or 4 non-haematological toxicity from prior therapies. Monitor closely for infections and administer antimicrobial medicines and Granulocyte-Colony Stimulating Factor as indicated. Gastrointestinal toxicity: anti-emetic, anti-diarrhoeal, and/or fluid/electrolyte replacement therapy as indicated, modify dose of Lonsurf as necessary. Lactose Intolerance. Hepatic impairment: not recommended if moderate or severe. Renal impairment: not recommended in severe or end-stage renal disease. Frequently monitor in moderate renal impairment for haematological toxicities. Elderly > 75 years. Children/adolescents under 18 years of age. Fertility not studied in humans. Pregnancy (Category D). Contraception: For women and men, must be used during treatment and for 6 months after stopping. Lactation: should not be used. **Interactions:** nucleoside transporters CNT1, ENT1 and ENT2, inhibitors of OCT2 or MATE1, human thymidine kinase substrates (e.g. zidovudine), hormonal contraceptives. **Ability to drive and use machines:** Possible occurrence of fatigue, dizziness or malaise. **Adverse Effects:** Very common: Neutropenia, anaemia, leukopenia, thrombocytopenia, diarrhoea, nausea, vomiting, fatigue, decreased appetite. Common: Lower respiratory tract infection, febrile neutropenia, lymphopenia, hypoalbuminaemia, dysgeusia, peripheral neuropathy, dyspnoea, abdominal pain, constipation, stomatitis, oral disorder, hyperbilirubinaemia, Palmar-plantar erythrodysaesthesia syndrome, rash, alopecia, pruritus, dry skin, proteinuria, pyrexia, oedema, mucosal inflammation, malaise, hepatic enzyme increased, blood alkaline phosphatase increased, weight decreased. Uncommon: Septic shock, infectious enteritis, lung infection, biliary tract infection, influenza, urinary tract infection, gingivitis, herpes zoster, tinea pedis, candida infection, bacterial infection, infection, upper respiratory infection, conjunctivitis, cancer pain, pancytopenia, granulocytopenia, monocytopenia, erythropenia, leukocytosis, monocytosis, dehydration, hyperglycaemia, hyperkalaemia, hypokalaemia, hypophosphataemia, hypernatraemia, hyponatraemia, hypocalcaemia, gout, anxiety, insomnia, neurotoxicity, dysaesthesia, hyperaesthesia, hypoaesthesia, syncope, paraesthesia, burning sensation, lethargy, dizziness, headache, visual acuity reduced, blurred vision, diplopia, cataract, dry eye, vertigo, ear discomfort, angina pectoris, arrhythmia, palpitations, embolism, hypertension, hypotension, flushing, pulmonary embolism, pleural effusion, rhinorrhoea, dysphonia, oropharyngeal pain, epistaxis, cough, haemorrhagic enterocolitis, gastrointestinal haemorrhage, acute pancreatitis, ascites, ileus, subileus, colitis, gastritis, reflux gastritis, oesophagitis, impaired gastric emptying, abdominal distension, anal inflammation, mouth ulceration, dyspepsia, gastrooesophageal reflux disease, proctalgia, buccal polyp, gingival bleeding, glossitis, periodontal disease, tooth disorder, retching, flatulence, breath odour, hepatotoxicity, biliary dilatation, skin exfoliation, urticaria, photosensitivity reaction, erythema, acne, hyperhidrosis, blister, nail disorder, joint swelling, arthralgia, bone pain, myalgia, musculoskeletal pain, muscular weakness, muscle spasms, pain in extremity, renal failure, noninfective cystitis, micturition disorder, haematuria, leukocyturia, menstrual disorder, general physical health deterioration, pain, feeling of body temperature change, xerosis, discomfort, blood creatinine increased, prolonged electrocardiogram QT, international normalised ratio increased, activated partial thromboplastin time prolonged, blood urea increased, blood lactate dehydrogenase increased, total protein decreased, C-reactive protein increased, haematocrit decreased. Post-marketing experience: interstitial lung disease. **Overdosage:** Consult Approved PI. **Pharmacological Properties:** Trifluridine is an antineoplastic thymidine-based nucleoside analogue and tipiracil hydrochloride a thymidine phosphorylase inhibitor. **Date of most recent amendment to Approved Product Information:** 02 December 2019. **Sponsor:** Servier Laboratories (Australia) Pty. Ltd. 8 Cato Street Hawthorn, VIC 3122. Material prepared December 2019.

For more information or to report an adverse event contact Medical Information on 1800 153 590.

**References:** **1.**Mayer RJ et al. N Engl J Med. 2015;372:1909-1919 **2.** Shitara K et al. Lancet Oncology 2018;19(11):1437-1448 **3.** Lonsurf Approved Product Information **4.** ESMO consensus guidelines for the management of patients wirh mCRC, Ann of Oncol 2016;27(8):1386-1422 **5.** www.PBS.gov.au

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ABSTRACTS

# Poster Abstracts

## PP1 | Investigations of an Epid-Based 3D Dose Reconstruction Method for Applications in MRI-Linac Radiotherapy

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**Background**: One of the challenges of external beam radiotherapy (EBRT) with conventional linacs is that tumours tend to move both between treatment fractions (interfraction motion) and during the treatment itself (intrafraction motion). The MRI-Linac could provide real-time tracking of tumours and better adaptive treatment planning accounting for both intrafraction and interfraction patient motion.[1] We aim to adapt a predictive fluence model and use this with images from an Electronic Portal Imaging Device (EPID) to reconstruct dose delivered to the patient on the Australian MRI-Linac system.

**Methods**: We utilise a fluence model that predicts the EPID dose,[2,3] as well as a patient dose reconstruction (PDR) algorithm[4] that back projects this dose to the patient plane and calculates the three-dimensional patient dose via a collapsed cone convolution method.

We will adapt the model and algorithm to calculate the patient dose for the Australian MRI-Linac system, accounting for the various differences including the magnetic field of the MRI, larger SAD and SDDs and the horizontal linac beam orientation.

**Results**: The PDR algorithm has been demonstrated to work on a conventional TrueBeam linac using some simple square field plans as well as two clinical IMRT plans.

A predictive fluence model for the Australian MRI-Linac has been created and optimized, and is being used alongside an adapted PDR algorithm to calculate dose delivered to the patient. Testing is currently underway to verify the accuracy of this dose reconstruction method.

**Conclusions**: MRI-guided radiotherapy has the potential to greatly improve image-guided radiotherapy for cancer patients. Once our testing of the dose reconstruction is completed, we will be able to verify the accuracy of doses delivered to patients during treatments on the Australian MRI-Linac system.

## PP2 | Population-Level Uptake of Moderately Hypofractionated Radiotherapy in the Treatment of Prostate Cancer

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**Background**: High-quality phase III evidence published in the past few years shows the non-inferiority of hypofractionated radiation therapy regimes compared to conventional regimes in the treatment of prostate cancer. Hypofractionation has significant added benefits to both the patient and the healthcare system, with a shorter treatment duration. Despite this, hypofractionation has not been universally utilised.

**Aim**: This study aims to investigate the variation in the utilisation of hypofractionation for the treatment of prostate cancer, in public and private treatment facilities in New South Wales (NSW) from 2014 to 2018.

**Methods**: Men with prostate cancer and without pelvic lymph node involvement, who received definitive external beam radiotherapy at one of 12 public, or five private, radiation oncology treatment centres (ROTCs) in NSW were identified. Data from public ROTCs were obtained for the 2015 to 2018 period from the NSW Cancer Registry, while private data were obtained for the 2014 to 2017 period from radiotherapy source systems. Data on the number and percentage of patients receiving conventional versus hypofractionated treatment at each ROTC were extracted. This was compared between each ROTC and between private and public facilities as distinct groups.

**Results**: Of the 3951 patients, who participated in the study, 2997 received treatment in public facilities and 954 received treatment in

private facilities. The number of patients who received hypofractionation at the end of 2018 in public facilities was 517 (17%) and at the end of 2017 in private facilities was 61 (6%). Assessment of individual ROTCs yielded dramatic results; use of hypofractionation ranged from 0 to 44% between ROTCs.

**Conclusions**: Despite the benefits of hypofractionation, its utilisation is low, particularly in private facilities. There are many factors that may be responsible for variability in hypofractionation use. The next steps will be to identify these factors, determine their relative contribution, then disseminate this evidence to practicing radiation oncologists.

## PP3 | Evaluation of glucoCEST Measurement at 3T: In Vitro and In Vivo

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**Background**: The role of glucose as a biomarker for tumour metabolic activity is routinely observed in fluorodeoxy-glucose positron emission tomography (FDG-PET). Despite being a 'gold standard' imaging modality for the diagnostic assessment of tumour malignancy, the use of ionizing radiation places certain restrictions on its use. The technique known as chemical exchange saturation transfer of glucose uptake (glucoCEST) may provide a non-ionizing alternative to the measurement of glucose metabolism in the brain. This technique may prove to be a valuable tool in the staging and follow up of patients.

**Aim**: To evaluate the sensitivity of glucoCEST MRI at 3 tesla (3T) clinical scanner in vitro using a phantom and in vivo human brain.

**Methods**: MRI was performed on a Siemens 3T MR scanner with 32-channel head coil and Siemens CEST sequence. For in vitro study, three tubes containing: 60 mL water; 60 mL water + 1 mL glucose (Dextrose D50) and 60 mL water + 2 mL glucose, respectively, were measured. For in vivo study, a 35-year-old healthy volunteer underwent glucoCEST MRI scan before and after drinking a sugar-based drink (25 g sugar/150 mL water) after a 15 min waiting time.

**Results**: GlucoCEST contrast measured in vitro was found to modulate with varying glucose concentration (0, 1 2%), demonstrating sensitivity of the method to D50 volume. No significant difference was observed in signal intensity of each phantom tube using conventional T2-weighted imaging. In vivo measurements demonstrated increased glucoCEST contrast in both white and grey matter in response to a sugar-based drink.

**Conclusions**: This study supports the potential use of Siemens CEST sequence at 3T for measurement of glucose uptake in tumour, where variation in glucose concentration between 1 and 2% was depicted in vitro with varying CEST contrast. Measurement of acute CEST changes in the brain in response to glucose consumption further supports this observation.

## PP4 | Rates of Procedural Anxiety during Radiotherapy Using a Mask In Patients with Head and Neck Cancer

Erin Forbes[1], Kerrie Clover[1,2], Greg Carter[1,2], Chris Wratten[3], Ben Britton[4], Minh Thi Tieu[3], Mahesh Kumar[3], Sharon Oultram[3], Amanda L. Baker[1] and Kristen McCarter[1]

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**Background**: During radiotherapy for head and neck cancers (HNC), patients are required to wear a tight-fitting immobilisation mask during treatment. Wearing the mask has been described by patients as one of the worst things about radiotherapy. However, there has been limited research into anxiety associated with this procedure. Our previous research at the Calvary Mater Newcastle, found patient anxiety can disrupt radiotherapy treatment sessions.

**Aim**: This study aimed to describe the prevalence of mask-related procedural anxiety during radiotherapy simulation and the first three radiotherapy treatment sessions.

**Methods**: This study was embedded within a larger study of anxiety in radiotherapy. Patients newly diagnosed with HNC attending the Calvary Mater Newcastle for radiotherapy were observed by a research assistant during simulation and a subset of treatment sessions (treatments 1, 2 and 3). The research assistant recorded disruptions (needing to remove the mask due to anxiety) or whether any intervention (anxiolytic medication) was required.

**Results**: The mean age of patients ($n = 101$) was 70 years and 76% were male. During simulation, 5.9% of patients required an anxiolytic and 4.9% of patients needed to remove the mask. During the first three treatments, 7.3% (T1), 8.9% (T2) and 6.6% (T3) of patients required a sedative; and 3.2% (T1), 2.3% (T2) and 2.24 % (T3) needed the mask removed. Overall, 8.9% of patients required a sedative during the first three treatments, and 4.9% of patients needed the mask removed during the first three treatments.

**Conclusions**: These findings suggest that a sizeable subset of patients experience intense mask-related procedural anxiety during radiotherapy for HNC. Pharmacological intervention to reduce anxiety during radiotherapy can be time consuming and is often not preferred by patients. The proportion of patients experiencing mask-related procedural anxiety during radiotherapy warrants further investigation to explore effective and acceptable alternatives.

## PP5 | Toward Safe Delivery of Radiation Therapy — Assessment of the Sensitivity of Clinically Used Patient-Specific Quality Assurance Methods

Joerg Lehmann[1,2,3], Mohammad Hussein[4], Therese Standen[1], Shankar Siva[5], Alisha Moore[6], Brindha Subramanian[7], Michael Barnes[1,2], Peter Greer[1,2] and Catharine Clark[4,8,9]

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**Background**: Quality of radiation therapy treatment has a major impact on patient outcomes, independently of other factors. Currently, the quality of complex modern intensity modulated treatments is examined at most radiotherapy clinics for every patient individually using a patient-specific quality assurance (PSQA). Methods and equipment used vary greatly between clinics. PSQA procedures are time consuming and costly, while their ability to detect clinically significant deviations of treatment quality is unclear.

**Aims**: This work aims to systematically and remotely test the sensitivity of clinics' PSQA procedures to detect clinically relevant treatment delivery problems.

**Methods**: A software tool has been created to edit radiation delivery instructions (DICOM plan files) and introduce small simulated errors. Participating clinics are invited to provide a treatment plan for a prescribed scenario. Using the tool, 12 versions of the plan with errors are created. The clinics are requested to perform their regular PSQA procedure for each of the plans, as well as our established method for remote auditing of centres for clinical trials (VESPA).

**Results**: In local preparation work, the simulated errors to be introduced into the clinics' plans have been carefully selected for their ability to result in clinically significant changes to the given treatment while remaining small enough to be otherwise potentially overlooked. Combinations of small errors with synergistic impacts have also been employed. Clinics using varying PSQA methods and located in Australia, the United Kingdom and the United States have enrolled and started measurements. Results received so far illustrate notable differences in the sensitivity of clinical PSQA systems.

**Conclusions**: This is the first study of its kind and its outcomes will ultimately be recommendations and strategies to improve the quality and consistency of radiation therapy across Australia/NZ and worldwide along with potential health cost savings and improvements to quality assurance in clinical trials.

## PP6 | A Multi-Centre Study of MRI-Only Prostate Radiation Therapy Planning: A NINJA Trial Sub-Study

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**Background**: Traditionally prostate radiation therapy has required 8 weeks of treatment. The multi-centre clinical trial Novel Integration of Novel Integration of New prostate radiation schedules with adJuvant Androgen deprivation (NINJA) is comparing new schedules of five daily treatments versus a longer regimen of 14 treatments. Radiation therapy for prostate is conventionally performed with MRI scans for prostate (target) delineation and CT scans for dose calculation purposes. However, this can introduce systematic registration errors in the treatment. In conjunction with NINJA, an MRI sub-study is being performed where patient treatments will be planned solely using MRI scans to improve the accuracy of the treatments.

**Aims**: To demonstrate the feasibility of MRI-only prostate planning within the context of a multi-centre trial.

**Methods**: The implementation model comprises three phases (1) retrospective: conventional workflow with comparison of the accuracy of MRI-only dose calculations; (2) prospective: MRI-only workflow with quality assurance comparison to conventional CT scan; (3) Full NINJA: MRI-only workflow with quality assurance to bulk anatomical density (BAD) dose calculation. For MRI-only workflow, a synthetic CT scan is computer generated from the patient MRI scans for dose calculations using an existing method.[1]

**Results**: To date, two centres have enrolled patients ($n = 14$) on the MRI sub-study with three patients at phase 3 Full NINJA. The first two patients at phase 3 required CT scanning due to unforseen issues, while the third became the first prostate treatment in Australia performed without a CT scan. All patients have achieved the stated quality assurance criteria for accuracy of dose calculations on MRI.

**Conclusions**: To date two centres have demonstrated the capability to perform MRI-only treatment planning for this trial. Other centres are expected to come on-line following MRI scanning equipment purchases.

## PP7 | Real-Time Assessment of Lung Depth and Skin Distance during Deep Inspiration Breath Hold (DIBH) Radiotherapy of Breast Cancer

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**Background**: Radiation treatment for breast cancer patients is nowadays often delivered with the patient holding their breath. This approach, referred to as Deep Inspiration Breath Hold (DIBH), aims to reduce the amount of radiation received by the patient's heart and lungs. Monitoring how well the patient holds their breath can be done using images formed by the treatment beam on an imaging panel placed on the beam exit side of the patient. Called electronic portal imaging devices (EPIDs), these panels are available on most modern treatment machines making this approach appealing as does its lack of any additional radiation dose to the patient.

**Aims**: This work aims to implement the previously tested method with a C#.NET software tool for robust clinical use. The tool will analyse EPID images acquired during breast cancer radiotherapy treatment in real time and report agreement with expected parameters to the treatment team.

**Methods**: The C#.Net tool is based on a MATLAB prototype, which had been tested offline on thousands of existing patient images, including those of the TROG 14.04 HART trial. In addition to the lung depth (distance between the posterior field edge and the lung — chestwall interface), the software will measure the distance from the posterior field edge to the skin, which was shown in previous work to be an additional reliable breath hold indicator.

**Results**: The first version of the C#.Net tool has been successfully tested on a clinical linear accelerator. It was able to read in live streaming images of a phantom placed on the treatment couch and to perform basic analysis of the profiles extracted from those images.

**Conclusions**: Measurements of inspiration levels of breast cancer patients during DIBH treatment using EPID images are expected to provide improved control of the treatment delivery without additional imaging dose and extra hardware.

## PP8 | Prevalence of Current School-Level Nutrition Policies and Practices of Secondary Schools in NSW, Australia

Jia Ying Ooi[1,2,3], Sze Lin Yoong[1,2,3], Rachel Sutherland[1,2,3], Jessica Wrigley[2], Christophe Lecathelinais[1,2,3], Kathryn Reilly[1,2,3], Lisa Janssen[2], Nicole Nathan[1,2,3] and Luke Wolfenden[1,2,3]

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**Background**: Lowering rates of adolescent overweight and obesity is a public health priority, as excess weight tends to track into adulthood, increasing the risk of a range of cancers and cardiometabolic diseases. Schools are an ideal setting to improve adolescent health and diet; however, there is little data assessing the implementation of evidence-based nutrition policies and practices in Australian secondary schools.

**Aims**: To investigate school-level nutrition policies and practices of secondary schools in NSW, Australia, and reported barriers and facilitators to implementation.

**Methods**: A two-part telephone survey consisting of a section for school principals and a section for school canteen managers was conducted on a cross-sectional sample of secondary schools in NSW, Australia. The survey was designed using the Centers for Disease Control and Prevention (CDC) Framework for addressing the school nutrition environment and services. Univariate analyses were used to assess differences in implementation by school sector, SES and location.

**Results**: A total of 137 school principals and 80 canteen managers completed the survey. School implementation for water, marketing and learning opportunities was high (>90%). Implementation of policy, canteens, fundraisers and staff training was reported in less than a quarter of participating schools. There were no significant differences in implementation by school sector, socioeconomic status and geographic location. Reported barriers were other priorities and commitments (28.47%), and lack of parental support (13.87%), and staff and student support (13.14%). Reported facilitators included support from stakeholders, staff, students and parents (37.23%), providing resources (30.66%), and financial aid (24.82%).

**Conclusions**: There is considerable opportunity to improve the implementation of nutrition policies and practices in secondary schools, particularly improving the availability of unhealthy options, staff training and nutrition policy implementation. Strategies to target barriers, such as gaining support from school staff, students and parents and provision of resources and funding, are needed.

## PP9 | A Cluster Randomised Controlled Trial of a Web-Based Intervention to Improve Child Dietary Intake within Childcare Centres

Courtney Barnes[1,2,3,4], Alice Grady[1,2,3,4], Amber E. Vaughn[5], Nicole Nathan[1,2,3,4], Luke Wolfenden[1,2,3,4] and Serene Yoong[1,2,3,4]

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**Background**: Poor dietary behaviours are the leading modifiable risk factor for the development of non-communicable diseases and specific types of cancers. As dietary behaviours developed during childhood track into adulthood, childcare centres are a promising setting for targeting children's nutrition behaviours. Research has identified

several childcare-based nutrition practices associated with improved child diet. However, such practices are not routinely implemented by childcare staff.

**Aims**: The primary aim of this study is to examine the impact of a web-based intervention targeting childcare centre nutrition practices on improving child dietary intake in childcare. Secondary aims are to examine the impact of the intervention on childcare centre implementation of nutrition practices.

**Methods**: A 6-month cluster randomised controlled trial will be conducted with 22 childcare centres within NSW, Australia. Centres allocated to the intervention group will receive access to a web-based program and health promotion officer support to implement nutrition practices to improve child diet in care. The primary outcome will be mean serves of fruit and vegetables consumed by children while in care, assessed through lunchbox measurements with 440 children. Self-reported centre implementation of nutrition practices and processes to meet nutrition practices will be assessed via interviews with centre supervisors.

**Results**: Twelve centres have been recruited to the study to date. Pilot testing of the web-based program and implementation support has been conducted with four childcare centre staff, indicating high feasibility and acceptability. Baseline self-reported centre implementation of the nutrition practices will be presented.

**Conclusions**: This study will provide current data on the prevalence of childcare centre implementation of nutrition practices. Results of the study are likely to inform future support strategies delivered to centres to support implementation to improve child dietary intake and reduce the future risk of cancer in children attending care.

## PP10 | A Pilot Study of a Video-Based Educational Intervention and Cervical Cancer Awareness amongst Senior High School Students in Ghana — A Before After Study

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**Background**: Cervical cancer is the second most common cancer and topmost cause of cancer deaths amongst women in Ghana. Cervical cancer screening in Ghana begins at 25 years; however, screening uptake is very low. High rates of information and communication technology use in Ghana present an opportunity for raising adolescents' cervical cancer awareness and screening uptake.

**Aim**: To assess the effect of a video-based educational intervention (VBEI) in improving awareness of cervical cancer and reducing barriers to cervical cancer screening amongst senior high school (SHS) students in Ghana.

**Methods**: A single-arm before and after study in which 50 respondents were selected using stratified probability sampling. Participants viewed a 20-min YouTube video on cervical cancer and self-completed a study-specific questionnaire before and after the VBEI. McNemar's test was used to test the difference in awareness between pre- and post-intervention at a significance level of $P < .05$.

**Results**: There was a statistically significant increase in awareness of the causative agent of cervical cancer ($P = .003$) and treatment outcomes ($P = .003$). However, there was no statistically significant change in awareness of risk factors ($P = .215$), signs and symptoms of cervical cancer ($P = .056$) or barriers to cervical cancer screening ($P = .322$).

**Conclusions**: This study provides preliminary evidence that VBEI may be an effective strategy for increasing awareness of cervical cancer. Future research should focus on developing and rigorously testing a culturally tailored video-based educational intervention to improve cervical cancer awareness and screening uptake amongst SHS students.

## PP11 | Bridging the Gap Between Research and Practice: A System for Knowledge Translation

Matthew McLaughlin[1,2,3,4], Alison Brown[1,2,3,4], Benjamin Elton[2,3], Sarah Young[2,3], Jessica Wrigley[2,3], Courtney Barnes[1,2,3,4], Rebecca Hodder[1,2,3,4], Rachel Sutherland[1,2,3,4] and Clare Desmet[2,3]

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**Background**: Knowledge translation (KT) aims to bridge the gap between research evidence and practice. Evidence suggests the increased use of research in practice may subsequently reduce chronic disease incidence (including cancer).

**Aim**: To embed a system of KT within an Australian local health district service, responsible for delivering evidence-based obesity prevention interventions in school and child care settings. Specifically, the system aims to establish a culture of KT to increase the awareness and use of research amongst identified key target audiences (e.g. school Principals).

**Methods**: A series of planning meetings were held between research staff ($n = 3$) embedded in the health service (July 2018-September 2018). A KT system was planned for a health promotion program within the Hunter New England local health district targeting schools and early childhood education and care (*Good for Kids, Good for Life*). The system comprised of KT 'champions' ($n = 9$) embedded across each project ($n = 7$) of the program, responsible for leading the development

of a KT plan. Executive support was granted by relevant health service managers for the KT system (September 2018-September 2019).

**Results**: The completion of KT plans for each project resulted in identification of three key priorities: (1) the strengthening of brand awareness, to establish *Good for Kids* as a leading health promotion group on children and young peoples' health; (2) the establishment of a community advisory group, facilitating co-production; and (3) the co-production with an external company of a digital platform to share research findings with key stakeholders using plain language summaries.

**Conclusions**: Such a KT system may be useful to develop a culture of KT, and thus, increase the uptake of research and effectiveness of practice. Subsequently, this may reduce chronic disease incidence (including cancer). Future research should focus on evaluating the effectiveness of each of the three priorities.

## PP12 | Do Technical and Further Education (TAFE) Students Intend to Change Their Health Risk Behaviours?

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**Background**: A high proportion of vocational education students engage in multiple health risk behaviours. Changing a single health risk behaviour reduces chronic disease burden but the benefits are amplified when multiple health risk behaviours are changed.

**Aims**: The aim of this study is to investigate the prevalence of health risk behaviours amongst vocational education students and to examine their intentions to change their health-risk behaviours.

**Methods**: Students from six TAFE campuses were surveyed in class via a computer tablet. The survey asked about the behaviours for which participants did not meet Australian health guidelines and about their intentions to change those health risk behaviours.

**Results**: To date, 545 participants have completed the survey. The majority were men and the average age is 23.5 years. The prevalence for smoking (37%), inadequate fruit intake (44.4%), inadequate vegetable intake (90.1%), risky alcohol consumption (62.3%) and physical inactivity (28.4%) were high. Participants were significantly least likely to report that they intended to reduce their alcohol consumption (13.8%) in the next 6 months and most likely to report that they intended to increase their physical activity (54.4%).

**Conclusion**: There are high rates of health risk behaviours in TAFE students, the design of interventions should take into account those behaviours they wish to change and how to motivate them to consider changing behaviours, they have less interest in modifying.

## PP13 | Implementation of Recommended Healthy Eating and Physical Activity Policies and Practices in the Family Day Care Setting

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**Background**: Childhood overweight and obesity increases the risk of chronic disease later in life including cancer. Supporting early childhood education and care services to implement healthy eating and physical activity policies and practices is recommended to reduce the risk of childhood obesity. While extensive research examining the implementation of such practices has been conducted in centre-based services, few studies have assessed implementation within the family day care setting.

**Aim**: The aim of this research was to describe the implementation of recommended healthy eating and physical activity policies and practices in a sample of Australian family day care services.

**Methods**: All family day care service providers (managing organisational structures) ($n = 16$) and a sub-sample of family day care educators ($n = 174$) located across the Hunter New England region of NSW, Australia participated in a telephone survey. Service providers were assessed on the implementation of 13 evidence-based healthy eating and physical activity policies and practices. Educators were assessed on seven of these practices. Descriptive statistics were used for analyses.

**Results**: The most prevalent practices implemented by both service providers and educators included ensuring educators have access to suitable physical activity equipment to encourage active play (>98%) and communicating with families when children's lunchboxes were not compliant with dietary guidelines (>80%). However, service providers reported low rates of implementation for the majority of policies, including the implementation of physical activity (31%) and small screen (19%) policies and having educators trained in the healthy eating and physical activity in children (19%).

**Conclusions**: Improving the implementation healthy eating and physical activity policies and practices in the family day care setting, as well as increasing training of educators, may reduce the risk of obesity and certain types of cancer over the lifetime. Future research establishing effective approaches to improve the implementation of evidence-based policies and practices is required.

## PP14 | Regulatory Roles of the lncRNA OVAAL on Cancer Cell Survival and Cellular Senescence

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**Background**: Long noncoding RNAs (lncRNAs) function in cancer pathogenesis and phenotypes through a diverse array of mechanisms that are not presently fully understood.

**Aim**: To investigate the functional significance of lncRNAs in resistance cells, we sought to find lncRNAs differentially regulated in cancer cells resistant to either TNF-related apoptosis-inducing ligand (TRAIL) or the Mcl-1 inhibitor UMI-77, agents that act through the extrinsic and intrinsic apoptotic pathways, respectively.

**Methods**: We generated melanoma cell sub-lines with acquired resistance to UMI-77 and TRAIL through prolonged exposure of melanoma cells to the agents. Comparative RNA sequencing analysis was carried out to identify differentially expressed lncRNAs in the resistant cells and their corresponding parental counterparts. RNA pulldown followed by mass spectrometry was employed to interrogate proteins that bound to identified lncRNAs.

**Results**: We identified a commonly up-regulated lncRNA, ovarian adenocarcinoma-amplified lncRNA (OVAAL), which was responsible for apoptotic resistance of cancer cells. OVAAL expression was significantly increased in colorectal cancer and melanoma compared with the corresponding normal tissues. Functionally, OVAAL silencing significantly inhibited cancer cell proliferation and retarded tumour xenograft growth. Mechanically, OVAAL physically formed ternary complex with serine/threonine-protein kinase 3 (STK3) and RAF proto-oncogene serine/threonine-protein kinase (Raf-1), which enhanced the activation of the RAF/mitogen-activated protein kinase kinase 1 (MEK)/ERK signalling cascade, thus, promoting c-Myc-mediated cell proliferation and Mcl-1-mediated cell survival. On the other hand, silencing of OVAAL triggered cellular senescence through polypyrimidine tract-binding protein 1 (PTBP1)-mediated p27 mRNA translation, which was regulated by competitive binding between OVAAL and p27 mRNA to PTBP1.

**Conclusions**: Taken together, these results reveal that OVAAL is required for the survival of cancer cells through dual mechanisms controlling RAF/MEK/ERK signalling and p27-mediated cellular senescence.

## PP15 | Anti-Acute Myeloid Leukaemia Properties of Low-THC Cannabis

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**Background**: Acute myeloid leukaemia (AML) is a lethal blood cancer for which elderly patients are often not of adequate health to receive standard treatment and succumb eventually. Cannabis has been used in the treatment of disease for thousands of years. The passage of the Controlled Substances Act (CSA) of 1970 (USA), led to its prohibition because of the side effects induced by psychoactive cannabinoid, tetrahydrocannabinol (THC). The recent introduction of research licenses investigating health benefits of cannabinoids promoted our interest in unravelling the anecdotal anti-AML effects of low-THC cannabis.

**Aim**: Examine the chemical compounds of low-THC cannabis extracts (cannabinoids and essential oils) influencing cell proliferation and cell death in in-vitro models of AML.

**Methods**: Utilising AML cell lines harbouring FLT-3-ITD (MV4-11) and NRAS (HL-60) mutations, and primary $CD3^{4+}$ bone marrow stem cells (BMSC), we examined anti-AML properties of crude cannabis decarboxylated ethanol extracts (CE), pure cannabinoids (CBD, THC) and crude essential oils/EO and pure terpenes (terpinolene, caryophylline) in in-vitro setting.

**Results**: Cell proliferation assays revealed that, MV4-11 cells were more sensitive to CE and pure cannabinoids (IC50: CE 3.8 μg/mL, CBD 1.9 μg/mL and THC 6.7 μg/mL) compared to HL-60 cells (IC50: CE 10.1 μg/mL, CBD 7.6 μg/mL and THC 16.2 μg/mL). HL-60 cells showed greater sensitivity to both crude EO and pure terpenes (IC50: EO 49.7 μg/mL and terpinolene 45.9 μg/mL) than MV4-11 cells (IC50: EO 137.5 μg/mL and terpinolene 148.9 μg/mL). Importantly, no cytotoxicity was observed in BMSC at concentrations of 12.5 μg/mL CE. Highly synergistic effects were seen with combined application of CE and crude EO or pure terpenes (IC50: CE 1.8 μg/mL and EO 36.9 μg/mL for MV4-11 and for HL-60 2.3 μg/mL and 44.9 μg/Ml, respectively) in both AML cell lines.

**Conclusions**: The safety and efficacy themes suggested by our results reveal the clinical potential of low-THC cannabis in AML treatment, particularly patients with poor prognosis. Work continues in our laboratory to test these chemicals using preclinical models.

## PP16 | Profiling the Immune System in Primary and Recurrent Glioblastoma

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**Background**: Immunotherapy has benefit in some solid tumours, including melanoma, where immune infiltration can be pronounced. Until recently, the central nervous system was thought to be immune privileged. Immune cells are capable of infiltrating tumours from glioblastoma patients, but immunotherapy trials have not consistently shown a benefit in these patients.

**Aim**: The aim of this study was to profile the immune system in primary and recurrent glioblastoma tumours.

**Methods**: Formalin-fixed paraffin-embedded sections of primary and matched recurrent tumours from 13 patients with glioblastoma were processed for immunohistochemical labelling of a range of immune cell markers. Immune infiltration was scored on digitally scanned immunolabelled sections using a categorical system of 0 (absent), 1 (present), 2 (moderate) and 3 (marked).

**Results**: Immune cells were observed in three topographical locations within primary and recurrent glioblastoma tumours namely the tumour proper, perivascular spaces and associated with haemorrhages within the tumour. $CD^{3+}$ cell infiltration into the tumour proper was present in almost all primary and recurrent tumours. However, only one case (case #9) had $CD^{3+}$ or $CD^{8+}$ cell infiltration scores >1 for both primary and recurrent tumour. Indeed, very low levels of immune infiltration were observed in most glioblastoma cases. $CD^{3+}$ cells were observed in perivascular spaces in 11 of the 13 cases for both primary and recurrent tumours. Only case #9 had $CD^{3+}$ cells in perivascular spaces that was scored >1 for both primary and recurrent tumours. Interestingly, $CD^{8+}$ cells were observed in perivascular spaces in 8 of 13 primary tumours but 12 of 13 recurrent tumours. Quantitative analysis of these and other immune markers is continuing.

**Conclusions**: In conclusion, while immune infiltration was observed in both primary and recurrent glioblastomas, the level of infiltration was quite low. This may correlate with the failure of some immunotherapy approaches in glioblastoma patients.

## PP17 | Targeting Transposable Elements for Analysis of Single-Cell DNA Methylation with Parallel Transcriptome Sequencing

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**Background**: Parallel analysis of the epigenome and transcriptome is a powerful method for unravelling cellular heterogeneity at single-cell resolution. Current methods utilise whole-genome bisulfite sequencing (scBS-seq), which is limited by low CpG coverage and poor mapping efficiency (approximately 10 to 40%).

**Aims**: To address these challenges, we aimed to develop a targeted single-cell sequencing method to estimate global DNA methylation levels. Single-cell Transposable Element Methylation sequencing (scTEM-seq) targets retrotransposons (LINE1 and SINE elements), which yields cost and time efficient estimation of average DNA methylation levels.

**Methods**: scTEM-seq was applied in KG1a cells treated with a hypomethylating agent (decitabine) for 72 hr.

**Results**: Using scTEM-seq, average mapping efficiencies for LINE1 and Sine Alu elements were 46.5 and 56.2%, respectively, and we recovered information from up to 400 and 1769 distinct annotations per cell. In untreated cells, the average DNA methylation measured by scTEM-seq was 81.1 and 81.9%, for LINE1 and Sine Alu, respectively. These values were within 2.8% of the genome-wide levels of DNA methylation obtained using a bulk cell method (79.1%). In cells treated with DAC, scTEM-seq libraries showed variable DNA methylation ranging from 31.7 to 67.4% and 31 to 80.7%, for LINE1 and Sine Alu, respectively. This heterogeneity was similar to data obtained using scBS-seq (range: 22.4-71.6%)

**Conclusions**: In summary, scTEM-seq provides accurate estimation of DNA methylation heterogeneity in single cells. Like scBS-seq, scTEM-seq can be combined with parallel transcriptome analysis. Thus, scTEM-seq will find applications where average levels of DNA methylation are of interest, rather than locus-specific DNA methylation patterns, for example, in cancer cells treated with hypomethylating agents or in induced pluripotent stem cells.

## PP19 | High Levels of the Protein Receptor EphA2 in the Blood of Brain Cancer Patients Undergoing Treatment for their Disease Predicts for Shorter Survival

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**Background**: Prognosis for people with brain cancer is dire. Standard treatment using the Stupp protocol prolongs survival but is not a cure. Blood-derived biomarkers provide an opportunity to better monitor therapy response. EphA2 (Ephrin type-A receptor-2) is a receptor protein overexpressed in brain tumours and is associated with disease progression and a poor prognosis.

**Aim**: To monitor circulating EphA2 levels in blood as a biomarker of disease progression in patients with brain cancer.

**Methods**: Plasma samples and survival data for 30 glioblastoma patients were obtained from the Hunter Cancer Biobank, NSW, Australia. Plasma EphA2 was detected using a commercial ELISA kit (Sigma-Aldrich) in 220 samples obtained before, during and after treatment with the Stupp protocol.

**Results**: The patient cohort included nine females and 21 males (median age: 61years, range: 18–81). The median survival was 442 days (range: 40–869) from first day of treatment. Plasma EphA2 concentration ranged from 0–20 ng/mL. The cohort was stratified into two populations designated as EphA2 negative or positive. Negative was an EphA2 concentration less than 0.15 ng/mL for the duration of the study ($n = 5$) or following treatment ($n = 5$). Positive was an EphA2 concentration greater than 0.15 ng/mL for the duration of the study ($n = 17$) or following treatment ($n = 3$). Of the EphA2 negative cohort, eight of 10 survived longer than the medium. Of the EphA2 positive cohort, seven of 20 survived longer than the median, three others survived but had not reached the median at the time of analysis, while 10 survived less than the median. Chi-square analysis comparing EphA2 negative and positive cohorts with survival less than or greater than the median showed a statistically significant difference ($P = .02$, odds ratio: 7.4).

**Conclusion**: The EphA2 negative cohort was 7.4 times more likely to survive longer than the median of 442 days compared with the EphA2 positive cohort.

## PP20 | A Simple Rapid HPLC Method for the Simultaneous Measurement of Temozolomide and Its Metabolite Levels in Glioblastoma Cancer Patients Plasma Samples

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**Background**: Glioblastoma (GBM) is the most common and lethal brain tumour. Standard treatment includes a combination of chemotherapy with temozolomide (TMZ) plus daily 6 weeks radiation (Stupp protocol followed by further chemotherapy alone). There is variable response to treatment including severe side-effects. TMZ is an antineoplastic agent with methylating properties and in-vivo activity via the decomposition product MTIC which rapidly degrades to the inactive derivative-5aminoimidazole-4-carboxamide (AIC). Dose individualization with chemotherapies has been shown to improve patient outcomes and minimise adverse events, yet dose individualization is a challenging task. Sensitive, rapid and reproducible methods to simultaneously measure drugs and metabolite levels in patient samples are needed to make it convenient and practical for patients and clinicians.

**Aims**: Develop a simple, sensitive and rapid HPLC-UV method for the simultaneous measurement of plasma TMZ and its metabolite AIC levels to recognize the degradation of TMZ and to predict for severe toxicity in blood samples from GBM patients treated with the Stupp protocol.

**Methods**: Internal standard teophyline (TP) was added to acidified plasma samples (200 μl) and ethyl acetate was added for extraction. Chromatographic separation was achieved using a Nova-pak CN 150 × 3.9 mm, 4 μm column with isocratic elution of mobile phase (10 mM ammonium phosphate, pH 6.5) with a flow rate of 0.5 ml/min. AIC and TP were detected at wavelength 276 nm and TMZ at 330 nm. Total run time was 9.0 min. The method is validated according to regulatory guidelines.

**Results**: The calibration curve is linear over a range of 0.2–20 μg/ml for TMZ and 1–20 μg/ml for AIC covering the expected concentrations in patient samples. The limit of quantitation is 0.1 μg/ml & 0.5 μg/ml for TMZ and AIC respectively.

**Conclusions**: This methodological improvement will facilitate the chemotherapy dose for each patient to be tailored to provide best response and reduced side effects.

## PP21 | Investigation of DNA Repair and the Epigenome in Chemoresistant High-Grade Serous Ovarian Cancer

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**Background**: Ovarian cancer is usually diagnosed at an advanced stage and has poor survival. One approach to address the low-survival rate is to find effective treatment options once chemoresistance occurs. The standard treatment for ovarian cancer is platinum chemotherapy such as carboplatin. DNA repair pathways, specifically nucleotide excision repair (NER) and homologous recombination (HR) recognise the damage and causes tumour cell death. We have previously found that high expression of ERCC1, which is part of the NER pathway, is associated with chemotherapy response, and low expression of ERCC1 with

resistance. DNA methyltransferase inhibitors (DNMTi) passively demethylate the genome, by blocking new methylation from occurring, allowing previously silent genes to be expressed. We hypothesize that when DNMTi is combined with carboplatin treatment, DNA repair pathways that may have been epigenetically silenced can be expressed, in turn recognising the damage caused by platinum chemotherapy, thus, resensitizing the tumour cells to the treatment.

**Aims**: The aim of the study was to determine if epigenetic therapies can resensitise ovarian cancer to platinum chemotherapy.

**Methods**: Molecularly characterised high-grade serous ovarian cancer cell lines were treated with sequential azacitidine and carboplatin. Response to treatment was determined by live-cell fluorescent assays to quantify apoptosis and cell death in real time. Transcripts of NER and HR pathways were quantified by TaqMan gene expression assays. MethylationEPIC array was performed to identify regions that have been demethylated, and whole transcriptome sequencing was performed to identify transcripts induced by sequential azacitidine and carboplatin treatment.

**Results**: Preliminary results indicate that the sequential treatment of low-dose azacitidine and carboplatin results in increased cell death and apoptosis, and reduced cell growth, compared to carboplatin only. This combination also increased the expression of ERCC1.

**Conclusions**: The potential outcome of this study will be effective new treatments for ovarian cancer patients that currently have very limited treatment options left.

## PP22 | MILIP is a Pan Cancer-Associated Long Noncoding RNA that Links MYC to Inactivation of p53

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**Background**: The involvement of noncoding RNAs (ncRNAs) in cancer pathogenesis has been increasingly appreciated. Although the expression and function of ncRNAs are highly tissue type- and context-dependent, we have found that long ncRNA (lncRNA) MILIP (Myc-inducible lncRNA inactivating p53) is commonly upregulated in TCGA cancer samples across 20 cancer types and that its high expression was associated with poor overall survival of patients.

**Aims**: To examine the functional significance of the lncRNA MILIP upregulation in the pathogenesis of cancer.

**Methods**: q-PCR and in situ hybridization (ISH) were used to examine the expression of MILIP in cell lines and human tissues, respectively. MILIP inducible knockdown cell sublines were established using the FH1tUTG I lentiviral vector. Colonogenic and CCK8 cell viability assays were used to reveal the impact of MILIP on cancer cell proliferation and survival.

RNA-seq data were subjected to ingenuity pathway analysis (IPA) and gene set enrichment analysis (GSEA) to identify downstream signalling pathways and target genes of MILIP. RNA immunoprecipitation (RIP) and RNA pull down were used to identify the binding between p53 and MILIP. Chromatin immunoprecipitation (ChIP)-seq was applied to investigate the role of MILIP in regulating p53 occupancy on genomic DNA. ChIP and luciferase reporter assay were applied to examine the occupancy and activation of *MILIP* promoter by c-Myc.

**Results**:

1. MILIP is a pan-cancer associated lncRNA responsive to c-Myc.
2. MILIP promotes cell proliferation and tumorigenicity.
3. MILIP regulates p53 occupancy on target promoters.
4. MILIP destabilizes p53 through facilitating its polyubiquitination.

**Conclusions**: Our results identified MILIP as a pan-cancer associated oncogenic driver and implicated that MILIP may constitute a target for treatment of diverse types of cancer.

## PP23 | Phosphoproteomics Uncovers Signalling Pathways Modulated by PP2A B55$\alpha$ in Breast Cancer

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**Background**: PP2A-B55$\alpha$ is a regulatory subunit of the ser/thr protein phosphatase 2A, and is a tumour suppressor in a range of cancers including breast cancer. Low gene and proteins level of PP2A-B55$\alpha$ (encoded by the PPP2R2A gene) are associated with aggressive breast tumours, and predicts for worse outcome in breast cancer patients. Our laboratory has shown that molecular inhibition of PPP2R2A enhances breast tumourigenesis; however, the pathways regulated by PPP2R2A are unknown.

**Aims**: Application of a phospho-peptide enrichment strategy and quantitative mass spectrometry to identify differentially activated proteins/pathways regulated by PPP2R2A loss in breast cancer.

**Methods**: Comparative phosphoproteomics was performed on BT474 cells (human luminal-B-like breast cancer), transduced with either control shRNA or shRNA sequences directed toward two different regions of the PPP2R2A. Titanium dioxide enriched phosphopeptides were sequenced and quantified by LC-MS/MS and differential proteins and pathways analysed using ingenuity pathway analysis software.

**Results**: A significant increase in phosphorylation of 56 sites from 48 proteins and decrease in phosphorylation of 24 sites from 22 proteins were identified in both of the PPP2R2A knockdown cell lines. These included PPP1R13L (a p53 inhibitory protein), AHNAK (a negative regulator of AKT and MAPK signalling) and YAP1, a transcriptional regulator involved in suppressing apoptotic genes, which were confirmed using phospho-PRM analysis. Key pathways that were affected by PPP2R2A knockdown included Rho-GTPAse and cell-cell junction signalling, which likely contributes to the increased metastatic capacity observed with PPP2R2A knockdown; and PI3K/AKT signalling pathways was mediated by PP2A, particularly activated by PPP2R2A knockdown.

**Conclusions**: PPP2R2A inhibition may contribute to breast cancer by altered activation of multiple proteins involved in P53, AKT, MAPK and ER signalling pathways. This study sheds light on the pathways regulated by this important tumour suppressor and paves the way for novel therapies for breast cancer patients.

## PP24 | In vitro Efficacy of the Dopamine Receptor D2 (DRD2) Antagonist ONC201, for the Treatment of Diffuse Intrinsic Pontine Glioma (DIPG)

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**Background**: Diffuse intrinsic pontine glioma (DIPG) is the most aggressive, childhood brain cancer with a poor median survival of 10 months. Remarkably, approximate 90% of DIPG cases harbour recurring point mutations in histone H3, inducing a lysine for methionine substitution at amino acid 27 (H3K27M), in either H3.1 (*HIST1H3B: 25%*) or H3.3 (*H3F3A: 65%*) variants. A recent case study showed ONC201, a dopamine receptor D2 (DRD2) antagonist currently in clinical trials for H3.3K27M+ glioblastoma, has utility in a patient with H3.3K27M mutant DIPG. Whether DIPGs harbouring H3.1 variants are sensitive to ONC201 is unknown.

**Aim**: This project aims to determine the sensitivities of DIPG tumours harbouring H3.1K27M and H3.3K27M mutations to ONC201, and to test the correlation between sensitivity and DRD2, DRD5 and H3K27M protein and mRNA expression.

**Methods**: Utilising a panel of eight DIPG patient-derived neurosphere cell lines harbouring wild-type H3 and mutant H3.1K27M and H3.3K27M, sensitivity to ONC201 was determined using cell proliferation and apoptosis assays. Protein expression and signal pathway examination was characterised via quantitative western blotting. mRNA expression was assessed by qPCR.

**Results**: ONC201 induced significant inhibition of growth and proliferation in 100% of H3.1K27M+ DIPG cell lines in vitro, compared to 50% of H3.3K27M+ DIPGs. No correlation between ONC201 sensitivity and DRD2 protein expression ($P = .8096$), or its negative regulator, DRD5 protein expression was seen ($P = .6279$). Whether ONC201 sensitivities correlate to other co-occurring molecular phenotypes in DIPG remains to be tested.

**Conclusions**: This is the first study to show that DIPG cells harbouring H3.1K27M are sensitive to ONC201. Unexpectedly, 50% of H3.3K27M DIPGs were refractory. Contrary to glioblastoma, ONC201 sensitivity did not correspond to DRD2 or DRD5 expression, suggestive of alternative mechanisms of action. Future studies will compare signalling processes driving resistance to identify biomarkers of sensitivity and guide DIPG treatment selection.

## PP25 | Characterising a New Target for the Treatment of Glioblastoma Multiforme

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**Background**: Glioblastoma multiforme (GBM) is the most common and aggressive primary brain tumour in humans. The median survival for GBM patients is 10–11 months and has remained static for decades, demonstrating an urgent need to investigate new targets for the treatment of GBM. A potential therapeutic target is brain and acute leukaemia cytoplasmic (BAALC) as it is expressed at low levels in normal tissue and is overexpressed in GBM, suggesting that it may be involved in tumourigenesis. The functions of BAALC in GBM have not been examined, however, BAALC plays a role in cell proliferation and survival in leukaemia cells. Novel BAALC inhibitors have been developed that specifically target BAALC, which may provide a more cancer cell-specific treatment, hence, they are important to examine.

**Aims**: The main aims of this study were to elucidate the cellular functions controlled by BAALC in GBM cells, and to examine the pre-clinical effectiveness of novel BAALC inhibitors in GBM models in vitro and in vivo.

**Methods**: BAALC expression was altered (siRNA knockdown, overexpression) in GBM cells. Effects on proliferation (resazurin), survival (Annexin) and migration (scratch assay) were measured ($n = 3$). A

panel of GBM cell lines were treated with increasing doses of BAALC inhibitors.

**Results**: We have shown that inhibition of BAALC expression in GBM cells increases cell death, while overexpression increases cell proliferation. Taken together, our data show that BAALC is involved in controlling GBM proliferation and survival. The BAALC inhibitors kill a range of GBM cell lines in vitro and were shown to be safe and well- tolerated in vivo.

**Conclusions**: There is an urgent need for new strategies for the treatment of GBM. Characterising BAALC, a potential therapeutic target, may provide a more cancer cell- specific treatment, which may reduce toxicity and side effects, resulting in improvement of patient survival.

## PP26 | The Role of the Tumour Suppressor PP2A-B55$\alpha$ in Epidermal Development

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**Background**: Protein phosphatase 2A is a family of serine/threonine phosphatase with diverse cellular functions. The regulatory subunit, PP2A-B55$\alpha$, has reported roles in cell division, migration, invasion and DNA damage repair, and functions as a tumour suppressor in a range of cancers. However, the functional role of this subunit in mammalian development is still poorly understood. To address this, we have generated the first knockout mouse model of PP2A-B55$\alpha$ (*Ppp2r2a* gene). Homozygous *Ppp2r2a* knockout caused embryonic lethality, with late-stage embryos displaying an epidermal barrier defect; however, the mechanism mediating this phenotype is not known.

**Aims**: To identify the functional role of PP2A-B55$\alpha$ in epidermal development.

**Methods**: PP2A-B55$\alpha$ protein expression was examined by immunofluorescence in wild-type (*Ppp2r2a*$^{+/+}$) and knock-out (*Ppp2r2a*$^{-/-}$) mice at embryonic days 14.5 (E14.5) and E18.5. The expressions of known and potential PP2A-B55$\alpha$ targets were examined by immunohistochemistry and immunofluorescence. Primary keratinocytes were isolated at E18.5 and proliferation and differentiation assessed.

**Results**: PP2A-B55$\alpha$ protein is highly expressed in the epidermis at E14.5 and decreases by E18.5 when the epidermal barrier has formed. In wild-type embryos between E14.5 and E18.5, an organised layer of basal stem cells progressively migrates and differentiates to form a highly organised stratified epidermis with the top layer (stratum corneum), acting as an impermeable barrier essential to post-natal life. In contrast, in *Ppp2r2a*$^{-/-}$ embryos at E14.5 the basal layer is highly disorganised and lacks proper apico-basal polarity. This disorganisation persists at E18.5, with thin, poorly differentiated outer layers. Expression of the phosphorylated forms of Akt and cJun, both essential for epidermal differentiation, are increased in *Ppp2r2a*$^{-/-}$ epidermis at E18.5. Wild-type keratinocytes proliferate in low calcium and terminally differentiate in high calcium. In contrast, *Ppp2r2a*$^{-/-}$ keratinocytes proliferated poorly and failed to differentiate.

**Conclusions**: We identify here an essential role for PP2A-B55$\alpha$ in epidermal development. The *Ppp2r2a*$^{-/-}$ phenotype suggests a crucial function for PP2A-B55a in apical-basal cell polarity and epithelial tissue architecture. As disruption of polarity is a key feature of epithelial tumours, this highlights a mechanism by which *PPP2R2A* loss can contribute to tumour development.

## PP27 | Empowering Aboriginal and Torres Strait Islander Women to Enhance Social and Emotional Well-being: Preparing to Pre-Test the MAMA-EMPOWER Mobile Phone App

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**Background**: Aboriginal and Torres Strait Islander women have expressed their need for direct and accessible health education and interventions when planning for pregnancy or when pregnant. Advanced technology, such as a mobile phone app, has been suggested as a source of innovation that could enhance the accessibility to better health outcomes and healthy lifestyles for mother and her baby. As high users of social media and technology, the potential to increase smoking cessation, nutrition and well-being could be enhanced through this app.

**Aims**: To develop and pre-test a tailored made, culturally appropriate mobile phone app 'MAMA-EMPOWER' for multiple behaviour change to empower Aboriginal and Torres Strait Islander woman through their pregnancy and/or pre-conception. This App will be tested for feasibility, appropriateness and useability.

**Methods**: Interviews and active user workshops were conducted iteratively with Aboriginal women. Using this information, a prototype app for multiple healthy behaviours and well-being has been led. A pre-test is being undertaken with Aboriginal and Torres Strait Islander women ($\geq$16 years pregnant and/or have a child/children <2 years). Women recruited from NSW communities will trial the app for 30 days and give feedback. Pre- and post-useability data will be collected via the app, through qualitative yarning circles and/or interviews. While the app is in use, women's changes of behaviours will be assessed.

**Results**: Decisions on the content focus and algorithms for prioritised messages will be presented, and preliminary pre-test results discussed.

**Conclusions**: Findings will inform the further need and development of a fully functioning App for Aboriginal and Torres Strait Islander women. This App will then be tested through a pilot RCT in Aboriginal communities. The significance of increasing smoking cessation during

pregnancy, decreasing alcohol consumption, improving wellness, nutrition and overall well-being will lead to improved health and lifestyle for mother, baby and families in Aboriginal communities.

## PP28 | Assessing the Potential Effectiveness of Dissemination Strategies on Uptake of an Evidence-Based Program to Improve Packing of Healthy Student Lunchboxes

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**Background**: Poor dietary intake is a leading risk factor for various cancers. As dietary habits in childhood track into adulthood, school-based nutrition interventions are a recommended cancer prevention strategy. While a range of effective school-based interventions exist, little evidence is available to support the population-wide uptake of evidence-based nutrition interventions in this setting.

**Aims**: This study aimed to assess the potential impact of a variety of dissemination strategies to enhance adoption of the SWAP IT healthy lunchbox program.

**Methods**: SWAP IT is an effective intervention comprised of nutrition curricula for school teachers, school-based guidelines and electronic messages pushed to parents of primary school-aged children via an existing school mobile communication app to improve the packing of healthy lunchboxes. Over a period of 12 months, researchers undertook a series of pre-post trials testing the impact of a variety of strategies to improve school uptake of the program. Project records and data from existing school databases were used to assess uptake and describe differences in the characteristics of schools adopting the intervention by dissemination strategy.

**Results**: Preliminary data suggest the most effective dissemination strategies were those where health promotion staff actively recruited schools through email and telephone contacts to Principals (33%), followed by presentations at Principal association meetings (32%), and when recruitment contact was undertaken electronically by the school mobile communication app provider (20%). Least effective were dissemination of recruitment information on the program website, stalls at education conferences and with school newsletter snippets (<5%). There were substantial differences in characteristics of schools recruited via each method, and costs of each recruitment strategy.

**Conclusions**: The findings suggest that active and direct dissemination methods are most effective in improving uptake of an evidence-based program to improve student nutrition. The effectiveness of such methods may be enhanced with the inclusion of multi-component approaches.

## PP29 | The Potential Role of Community Managed Organisations in Reducing Behavioural Risk Factors for Cancer amongst People with a Mental Health Condition

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**Background**: People with a mental health condition have a reduced life expectancy of 12–16 years in Australia compared to the general population, with cancer estimated to be responsible for 13% of this excess mortality. The prevalence of cancer risk behaviours, including poor nutrition, physical inactivity and harmful alcohol consumption, are up to two times higher amongst this group compared to the general population.

**Aims**: The 'CMO Connect' project aims to explore the role that community managed organisations (CMOs) may play in providing preventive care by identifying: (1) current CMO preventive care practices; (2) barriers and facilitators to CMOs providing preventive care; (3) consumer preferences for receiving preventive care and (4) the organisational mechanisms that may support systematic preventive care provision.

**Methods**: The project is utilising a codesign method, with both qualitative and quantitative data collection via an online survey of all CMOs in NSW; telephone interviews with people with mental health conditions; and online survey of CMO staff; and focus groups and research involvement with all stakeholders throughout the project; and a pre-post preventive care intervention pilot study.

**Results**: Preliminary analysis from the online survey with leaders of CMOs indicates that the majority (83%) are providing support to help consumers modify **at least one risk behaviour**; and approximately half are providing at least some of these consumers with support to **modify all risk behaviours** (49%). Subsequent sub-studies with CMO staff and consumers will assist in providing a more comprehensive picture of the preventive care that is currently being provided.

**Conclusions**: Following the exploratory studies and subsequent pilot study, the project will be able to recommend a feasible model of care provision that could further be tested, and potentially adopted and implemented by CMOs to help them reduce the inequitable risk of developing cancer experienced by people with a mental health condition.

## PP30 | Uptake of Proactively Offered Online and Telephone Interventions Targeting Health Risk Behaviours amongst Technical and Further Education (TAFE) Students

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**Background**: Online and telephone services are effective in improving health risk behaviours. However, uptake of such services is poor amongst the general population. Whilst rates of health risk behaviours amongst vocational education students are high, whether they sign-up to proactively offered online and telephone support services for more than one health behaviour is unknown.

**Aim**: This study aims to examine the uptake of online and telephone services for health risk behaviours amongst TAFE students.

**Methods**: As part of an electronic intervention offered via a computer tablet to vocational education students, online and telephone services were proactively offered to participants who did not meet Australian health guidelines for smoking, fruit and vegetable intake, alcohol consumption and physical activity. Uptake was measured by whether participants signed-up to the support services they were offered.

**Results**: To date, 593 vocational education students have been recruited. The majority are men and the average age is 26.2 years. Uptake of online services was 17% or less. For the telephone services, the uptake was 14% or less.

**Conclusion**: Vocational education students appeared in general to prefer online programs rather than telephone services to address their health risk behaviours, but uptake for both was low.

## PP31 | Eating in the USA: An ECR's Guide to International Collaboration

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**Background**: Malnutrition in cancer is widespread and related to poorer outcomes including mortality. This is particularly true in head and neck cancer patients who endure multiple impairments to their ability to consume adequate nutrients and hydration. Malnutrition while receiving radiotherapy for head and neck cancer is an independent predictor of mortality. To address this, Eating As Treatment ("EAT") an intervention to improve adherence with dietetic advice was developed and tested nationally via multi-centre trial. The success of the intervention in reducing malnutrition, weight loss, and radiotherapy interruptions resulted in international interest in the intervention from health and research institutions. However, translation of an intervention, particularly a behavioural intervention tailored for a specific population, is not a simple undertaking. Differences in cultures, settings, medical and research systems all affect the implementation of an intervention. Further, international collaboration, with multiple stakeholders, many of whom are very senior, creates unique challenges for the early career researcher.

**Aims**: This article aims to provide a guide for early-career researchers forging international collaborations. It details the opportunities and challenges of working with, and in non-Australian institutions.

**Methods**: The investigation will use as an example the author's collaboration with Yale School of Medicine (New Haven, CT, USA) examining whether EAT can be successfully translated to clinicians and patients based in the United States. International collaboration pitfalls, strengths, and practical stratagems for early career researchers will be presented from the perspective of a clinical psychologist and behaviour change expert.

**Conclusions**: EAT is an efficacious intervention, like many interventions developed by early career researchers. However, unless interventions can be disseminated and implemented their benefits will go unrealised. Therefore, collaboration outside of the early career researcher's own institution and indeed own country, has the potential to impact on the health and well-being of a greater number of people.

## PP32 | Detection of an IKZF1$^{Plus}$ Paediatric B-ALL and the Impact on Clinical Management: A Case Study

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**Background**: We report on the diagnostic cytogenomic findings of a 7-year-old female presenting with B-cell acute lymphoblastic leukaemia (B-ALL) and their impact on the clinical management. Full-blood count on presentation revealed anaemia and neutrophilia with the presence of circulating B-cell blasts confirmed by flow cytometry. Bone marrow aspirate morphology showed a diffuse population (75%) of lymphoblasts, which was consistent with B-lymphoblastic leukaemia/lymphoma.

**Methods/Results**: Conventional cytogenetic testing was performed on her bone marrow using G-banded karyotype and FISH studies, which showed normal results. In addition, a routine SNP-microarray was performed, which revealed sub-microscopic deletions consistent with the new B-ALL subtype IKZF1.$^{Plus}$

**Conclusions**: The IKZF1$^{Plus}$ subtype of B-ALL is defined by an *IKZF1* deletion with one or more concurrent deletions of *CDKN2A/B*, *PAX5*, *CLRF2-P2RY8* del/fusion and without the presence of an *ERG* deletion. Patients with *IKZF1* deletions have been shown to have a higher risk of relapse and those with an IKZF1$^{Plus}$ genomic profile have an even higher risk of relapse irrespective of MRD response by quantitative PCR.

With the implementation of SNP-microarrays, we were able to determine that this patient was in a high genomic risk category with a significantly increased risk of relapse at diagnosis. The patient has subsequently had their treatment intensified and in consolidation is stratified into the early high risk treatment group.

## PP33 | Enter the Matrix to Uncover Potential New Biomarkers for the Initial Stages of Ovarian Cancer Development

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**Background**: Ovarian cancer (OvCa) is the deadliest gynaecological cancer with 5-year survival of around 40%. The extracellular matrix (ECM), a three-dimensional protein structure that organises cells within a tissue, becomes abnormally expressed in cancer. Therefore, it is important to define the ECM composition of normal tissue to study how pathological ECM changes are involved in cancer development and progression. In high-grade serous ovarian cancer, the fallopian tube is suspected as the site of origin; however, the normal ECM composition of the human fallopian tube has not been comprehensively characterised.

**Aims**: To characterise the ECM composition of the human fallopian tube and to understand how the ECM affects normal and cancerous epithelial cells.

**Methods**: Human patient fallopian tube tissues ($n = 8$) were enriched for ECM and analysed using mass spectrometry. We next examined the influence of a novel ECM glycoprotein, *EFEMP1* (EGF-Containing *Fibulin*-Like Extracellular Matrix Protein 1), on fallopian tube biology using a *Efemp1* knockout mouse (KO) model supported by organoids.

**Results**: The fallopian tube ECM profile was comprised of 147 matrisome proteins from a possible 1027 known human ECM proteins. Many ECM genes are altered in human ovarian cancer. For example, *EFEMP1* genetic alterations in 5% of cases of human ovarian serous cystadenocarcinoma. *Efemp1* expression was more pronounced with age as indicated by RNA in situ hybridization showing increased *Efemp1* mRNA expression in oviducts of wild-type aged mice compared to young mice ($n = 3$). We found that knocking out this single ECM protein caused defective oviductal morphology particularly in aged mice. We are currently investigating the effect of the *Efemp1* deletion on oviductal secretory and ciliated cell dynamics using immunofluorescence and quantitative PCR ($n = 3$).

**Conclusions**: Our study is the first to present a comprehensive proteomic profile of the human fallopian tube ECM. Given the ECM is known to play a crucial role in cancer development, profiling the ECM landscape of the fallopian tube will reveal novel biomarkers to investigate the initial stages of ovarian cancer development and may lead to a new paradigm of treatment for this deadly disease.

## PP34 | Endoplasmic Reticulum Stress Drives Tumour Axonogenesis in Pancreatic Cancer

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**Background**: Every year almost as many people die from pancreatic cancer as are diagnosed. The poor survival rate and prognosis of the disease is associated with increased nerve infiltration into tumours. However, the molecular mechanisms by which cancer cells stimulate nerve infiltration remains unclear.

**Aims**: Our preliminary data show that nerve outgrowth is increased when neuronal cells are cultured with growth medium from endoplasmic reticulum stressed pancreatic cancer cells. This indicates that pancreatic cancer cells secrete molecules that induce nerve infiltration upon induction of ER stress. This study aims to detail the soluble

factors released by ER stressed pancreatic cancer cells, and assess their impact on neurite axonogenesis.

**Methods**: The conditioned growth medium from pancreatic cancer cells was analysed (using ELISA and mass spectrometry techniques) to profile all of the secreted factors from pancreatic cancer cells upon induction of ER stress. The impact of the candidate-secreted factors on neurite axonogenesis was assessed to determine the factors functional role in tumour nerve infiltration.

**Results**: Amongst the secreted factors altered in the ER stressed conditioned medium compared to the control, the level of proBDNF was significantly upregulated. Functional studies showed that introduction of recombinant human proBDNF recapitulated the enhanced neurite outgrowth mediated by ER stress-conditioned medium, whereas, inhibition of proBDNF by neutralizing antibody blocked nerve outgrowth.

**Conclusions**: Collectively, these results identify that proBDNF released by ER stressed-pancreatic cancer cells promotes nerve infiltration. This finding opens the door for targeting proBDNF in pancreatic cancer to prevent tumour nerve infiltration and the associated cancer growth.

## PP35 | Prostate-Specific Membrane Antigen Expression in Primary and Recurrent Glioblastoma

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**Background**: Patients with glioblastoma almost always suffer a recurrence of an aggressive treatment resistant tumour and succumb within months, highlighting the need to develop treatment options for recurrent glioblastoma. One potential target is prostate-specific membrane antigen (PSMA), expressed on newly formed blood vessels in primary glioblastoma tumours.

**Aim**: The aim of this study was to identify the extent of PSMA expression in primary and recurrent glioblastoma tumours and test whether expression increases in recurrent tumours.

**Methods**: Formalin-fixed paraffin-embedded sections of primary and matched recurrent tumours from 13 patients with glioblastoma were processed for PSMA immunohistochemical labelling. PSMA expression was scored from digitally scanned sections using a categorical system (total PSMA expression = PSMA label intensity (0-3) × percent PSMA-positive blood vessels). Total PSMA expression scores ranged from 0 to 230 (maximum score = 300) and was divided into low and high expression based on a median split (median = 57) of PSMA expression across all tumours.

**Results**: PSMA was localised to blood vessels in 12 of 13 primary and 9 of 13 recurrent glioblastoma tumours. Regression analysis showed a significant difference in PSMA expression between primary and recurrent glioblastoma ($P = .04$) with PSMA being highly expressed in approximately 70% of primary and only 31% of recurrent glioblastoma. Three cases displayed high expression in both primary and recurrent glioblastoma and one case had no PSMA expression at all.

**Conclusions**: In conclusion, while higher expression of PSMA was detected in more primary tumours, 70%+ of all primary and recurrent tumours expressed PSMA to some extent adding evidence that this may be a useful target for treatment of glioblastoma. Larger cohorts and other techniques for detecting PSMA are needed to provide further evidence for PSMA's utility as a target and to further define which glioblastoma patients are most likely to benefit from this approach.

## PP36 | Vault RNAs Have a Functional Role in Prostate Cancer

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**Background**: Prostate cancer has one of the highest incidence of all cancers in Australia. New treatments are required to improve outcomes and quality of life for patients. Extracellular vesicles (EVs) are secreted from their tissue of origin and recoverable from most bodily fluids. We previously found the abundance of vault RNAs in EVs could distinguish between prostate cancer and metastatic disease. However, the functional role of these non-coding RNAs is poorly understood and particularly their function in EVs in metastasis.

**Aims**: To investigate the EV associated function of vault RNAs and their fragments in prostate cancer.

**Methods**: The abundance of the fragments of vault RNA1-1 and vault RNA1-2 was determined by qPCR in EVs from prostate cancer cell lines. The functions of vault RNAs was investigated by transfection of the full-length RNA and fragments and siRNA to reduce the expression of the vault RNAs, into prostate cell lines and assessment of the alteration to cellular function using in vitro assays.

**Results**: There were differences in abundance for the different fragments of vault RNAs within EVs of metastatic prostate cell lines. Assessment in patient serum-derived EVs also identified variation, suggesting potential as a biomarker and a possible functional role in metastasis. In particular, the RNA fragment derived from the central portion of the vault RNAs showed lower abundance than the fragments derived from the 5' and 3' ends. Transfection studies have revealed that vault RNAs may have roles in prostate cancer cell survival.

**Conclusions**: EV associated vault RNAs are potential biomarkers for metastatic prostate cancer and also have a functional role in cancer

progression. Further work is ongoing investigating functions of these transcripts in EVs, confirming their biomarker potential in patient serum samples and their potential as targets for the development of new treatments.

## PP38 | Using Experimental Mouse Models to Understand the Pathogenesis of Lung Adenocarcinoma

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**Background**: Lung cancer (LC) is the fifth most commonly diagnosed cancer in Australia and is a leading cause of cancer-related morbidity and mortality not only in Australia but worldwide. Currently, there are two major hurdles in LC treatment and management. First, LC is diagnosed when it is at an advanced stage or has been metastasised. Second, although the genetic alterations responsible for lung adenocarcinoma are known, little is known about those that lead to the development of adenocarcinomas from adenomas. This is again due to the lack of proper diagnostic technique that enables early diagnosis. In this regard, mouse models serve as a valuable tool to understand LC development, as tumour tissue can be collected at different stage of LC development.

**Aims**: Establishing a mouse model for lung adenoma and adenocarcinomas using tobacco carcinogen/cigarette-smoke as carcinogen. Identifying genetic alterations linked to the development of lung adenocarcinoma using long-term mouse model and validate them in short-term mouse models (adenoma) and clinical samples.

**Methods**: A/J mice were administered a tobacco carcinogen, NNK (4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone), exposed to cigarette smoke (CS) for varying periods. Whole genome sequencing (WGS) was performed on tumour and non-tumour lung tissue and we are currently validating the WGS results to identify the mutations responsible for development of LC.

**Results**: In the short-term mouse model, 100% of mice exposed to NNK and 8-week of CS followed by 8-week of air rest develop adenomas resembling human bronchoalveolar adenomatous hyperplasia .These adenomas further progress to adenocarcinomas that resembles human bronchoalveolar carcinomas with increase in the duration of CS (12 weeks and more).

**Conclusions**: We have developed a novel mouse model that develops both lung adenomas and adenocarcinomas. We anticipate that the genetic analysis of tumours from these models would help to elucidate molecular mechanisms responsible for the development/progression of LC and identify early mutations that can be used diagnostically.

## PP39 | The Value of Panel Testing for the Identification of Women with a Genetic Predispostion to Breast or Ovarian Cancer

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**Background**: There are a number of well-characterized genes that predispose to the development of breast and or ovarian cancer. These include *BRCA1*, *BRCA2*, *PALB2*, *TP53*, *PTEN* and one common variant in *ATM*. There is unequivocal evidence that harbouring a causative change any one of these genes significantly changes the probability of a woman being diagnosed with disease. Unfortunately, this constellation of genes does not include many women who have a family history of disease. With the advent of panel testing, we are now able to test for a much larger number of genes in this population of women but precise advice as to their actual risk remains to be determined.

**Aim**: The aim of this study was to determine from a panel of up to 39 cancer susceptibility how many could be linked to breast and or ovarian cancer risk.

**Methods**: A total population to 1300 women, all screened for *BRCA1*, *BRCA2*, *PALB2*, *TP53*, *PTEN* and *ATM* causative variants were included in this study. As part of their screening either a 27 or 39 gene panel was used to identify genetic risk factors that could be associated with their disease.

**Results**: The results of this study revealed that over 10% of the total number of patients in this study harboured causative variants that were potentially pathogenic in nature. A number of variants were identified in genes not normally associated with breast cancer risk, especially those that are known to predispose to colorectal cancer, these included *MSH6*, *MSH2* and *APC*. There was also a variety of ATM pathogenic variants identified, which suggests the current screening strategy for ATM needs to be expanded to include all causative variants and not just the current single common variant.

**Conclusions**: The identification of causative genetic variants in a variety of genes further supports the notion that genetic screening for hereditary breast and ovarian cancer susceptibility should be expanded. With more knowledge about the genetic causes of disease, additional women can be offered the benefits of risk prediction so that

they can benefit from early intervention and appropriate prophylactic measures.

## PP42 | The Use of PARP Inhibitors in Glioblastoma

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**Background**: Glioblastoma multiforme (GBM) is the most aggressive form of brain cancer having a median survival of ~15-months with current treatments including surgery, radiotherapy and chemotherapy with the alkylating agent temozolomide. Treatment options for GBM have remained largely stagnant for decades as few drugs able to effectively penetrate the blood-brain barrier. Therefore, the identification of new treatments is urgently required. Poly (ADP-ribose) polymerase (PARP) is involved in DNA repair and is utilised by cancer cells to reverse the damage caused by chemotherapy. PARP inhibitors are currently indicated for the treatment of ovarian cancer; however, their potential benefit in the treatment of GBM has not been fully explored.

**Aim**: To determine whether PARP inhibitors are effective as anticancer agents for GBM, alone and in combination with temozolomide.

**Methods**: A panel of GBM cell lines were treated with the PARP inhibitors veliparib (ABT-888), olaparib (AZD2281), pamiparib (BGB-290) and niraparib (MK-4827) alone, or in combination with temozolomide. Cell viability was assessed using a resazurin assay and apoptosis and cell cycle analysis were assessed using flow cytometry.

**Results**: Treatment of GBM cell lines with PARP inhibitors led to a reduction in cell viability and enhanced the effects of temozolomide treatment. Further, PARP inhibitors were able to induce apoptosis and a cell line specific S-phase or G2/M-phase arrest at 24, 48 and 72h timepoints.

**Conclusions**: PARP inhibitors show efficacy against GBM cell lines, and enhance the effect of temozolomide *in vitro*, demonstrating that a combination of PARP inhibitors and temozolomide, given concurrently, may provide favourable treatment outcomes for GBM patients.

## PP43 | The Role of the Gastrointestinal Microbiome in Lung Cancer Pathogenesis

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**Background**: Lung cancer is the leading cause of cancer-related mortality in Australia, and cigarette smoke contributes to approximately 85–90% of cases. The gastrointestinal microbiome, defined as the sum of all microbes, their genomes and metabolites, is a key mediator of host immune responses including in the lungs. Several cancers (colon, pancreatic, liver breast) are linked to changes in microbiome composition and metabolism, and modulation of the gut microbiome protects against tumorigenesis in distal organs. Nevertheless, neither the role of the microbiome in the pathogenesis of lung cancer has not been characterised, nor has its therapeutic potential.

**Aims**: We aimed to characterise changes in microbiome composition and metabolism in a murine model of cigarette smoke exposure.

**Methods**: Female c57BL/6 mice were exposed to cigarette smoke for 12 weeks. Faecal microbiome composition was quantified by shotgun sequencing, and lung, plasma and caecum content metabolites were quantified by ultra high performance liquid chromatography-tandem mass spectrometry. Disease severity assessed by airway inflammation (bronchoalveolar lavage fluid (BALF)), histopathology (inflammation, alveolar destruction collagen deposition) and lung function (Flexivent; Scireq, CAN). Dietary modification of microbial metabolites was performed by feeding mice a diet high in resistant starch (SF11-025).

**Results**: Cigarette smoke significantly altered the composition of the gastrointestinal microbiome composition. This corresponded to changes in microbial metabolites in lung tissue, plasma and caecum contents including increased carcinogenic secondary bile acids in lung tissue, and reduced tumour-suppressing lactate and short chain fatty acids (SCFAs) in caecum contents. Increased dietary starch restored SCFA levels and reduced cigarette smoke-induced inflammation and pathology.

**Conclusions**: Cigarette smoke induced significant changes in gastrointestinal microbiome composition and metabolism, which may be associated with lung cancer pathogenesis. Dietary modification improved SCFA availability and protected against changes in lung pathology. Ongoing studies aim to validate these findings in mouse models of lung cancer and human lung cancer patients.

## PP44 | Oncogenic Upregulation of the Long Noncoding MIR4435-2HG in Pancreatic Cancer

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**Background**: Based on bioinformatic analysis of the Cancer Genome Atlas (TCGA) datasets, we found that the long non-coding RNA (lncRNA) MIR4435-2HG was commonly upregulated in pancreatic cancer compared with corresponding normal tissues and high MIR4435-2HG expression was associated with poor progression free survival (PFS) and overall survival (OS) of pancreatic cancer patients.

**Aim**: To examine the functional significance of MIR4435-2HG upregulation in the pathogenesis of pancreatic cancer.

**Methods**: Human pancreatic cancer cell lines carrying an inducible MIR4435-2HG shRNA system were used as tools to investigate the effect of MIR4435-2HG silencing on cell survival and proliferation. The results were confirmed by overexpression of MIR4435- 2HG. RNA sequencing analysis was carried out to identify potential downstream targets of MIR4435-2HG. RNA pulldown followed by mass spectrometry and RNA immunoprecipitation were used to interrogate RNAs and proteins binding to MIR4435- 2HG. The functional significance of the interaction between MIR4435-2HG and its binding partners was examined by combined knockdown and overexpression.

**Results**: MIR4435-2HG was frequently upregulated in pancreatic cancer patient samples and cultured cell lines in comparison with the corresponding normal tissue and normal cell lines, respectively, and promoted pancreatic cancer cell survival and proliferation. Ingenuity Pathway Analysis (IPA) of RNA sequencing data showed that knockdown of MIR4435-2HG significantly activated the IFN/STAT signalling pathway in pancreatic cancer cells.

**Conclusions**: The MIR4435-2HG plays an important role in promoting pancreatic cancer cell survival and division. This is associated with its regulatory effect on IFN/STAT signalling that conceivable impinges on the interaction between pancreatic cancer cells and their microenvironments.

## PP45 | Analysis of Febrile Neutropenia (FN) Rates According to (Neo)adjuvant Breast Cancer Chemotherapy Regimen Use

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**Background**: (Neo)adjuvant breast cancer chemotherapy regimens are associated with relatively high rates of FN. Pegfilgrastim, a granulocyte-colony stimulating factor (GCSF), reduces the risk of FN, however the optimal approach to patient selection for GCSF is unknown.

**Aims**: We conducted a retrospective review of patients treated with (neo)adjuvant breast cancer chemotherapy at a single centre, of FN rate according to chemotherapy regimen, nadir-neutropenia directed GCSF use, tumour and patient factors. We aimed to identify factors associated with a low rate of FN without nadir-directed GCSF.

**Methods**: Demographic, tumour and treatment data were collected from electronic patient records. FN rate in patients who received secondary-GCSF after cycle 1 nadir-neutropenia ($<1.0 \times 10^9$ cells/L) was compared with those who did not have a nadir blood in count cycle 1.

**Results**: Between 11/4/2011–22/4/2018, 584 patients received (neo)adjuvant chemotherapy. 315 patients did not receive primary-GCSF, of whom 238 had a cycle 1 nadir measurement and 133 had nadir-neutropenia. All regimens except weekly paclitaxel had rates of nadir-neutropenia >65%. 124 patients proceeded to receive nadir-neutropenia directed secondary-GCSF of which 6 developed FN (anthracycline 1/3, anthracycline-taxane(8) 0/27, TC 3/70, TCH 1/20, other 1/4). There were 78 patients who did not receive primary-GCSF and did not have a nadir measurement. Of 50 patients who proceeded to cycle 2 without nadir-neutropenia directed GCSF, none developed FN. Weekly paclitaxel comprised almost half of this group (22/50). There was no significant difference in rates of FN in patients who received nadir-neutropenia directed secondary-GCSF (6/124, 4.8%, 95% CI 1.1-8.6) compared with those who did not have a nadir measurement (0/50, 0%) ($p = 0.1135$).

**Conclusions**: In this population, nadir blood counts did not contribute to reduced rates of FN however there was unequal distribution of regimens across groups and very high rates of primary-GCSF usage.

## PP46 | Investigating the Use of Mitochondria-Targeted $H_2S$ Donors for the Treatment of NSCLC

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**Background**: Lung cancer (LC) is the fifth most common cancer diagnosed in Australia, yet it is the leading cause of cancer death. Non-small cell cancer (NSCLC) accounts for 83% of all newly diagnosed lung cancers and 70% of these diagnoses have advanced disease. There are several current treatment options for NSCLC including chemotherapy, surgery and more recently, targeted therapies such as EGFR TKIs.

However, the 5-year survival rate for lung cancer is less than 14% despite recent advancements in therapy, demonstrating an urgent need for more effective treatments.

**Aims**: We hypothesise that immune and metabolic pathways can be targeted with novel or repurposed drugs to assess their therapeutic potential in a novel NNK/CS-induced mouse-model of NSCLC. The aim of this project is to investigate the role of oxidative stress and mitochondria-targeted $H_2S$ donors (AP39/RT01) in the treatment of NSCLC.

**Methods**: A novel mouse model of lung adenoma was used to investigate the efficacy and mechanism of action of AP39 and RT01. At endpoint, lung function was measured before blood and lungs were collected. The left lobe of the lung was collected for histological analysis including immunofluorescence and immunohistochemistry. The multi-lobe lung was collected for molecular analysis including qPCR. All other organs were collected upon endpoint for future analyses of metastases.

**Results**: Treatment with AP39 and RT01 did not show any significant decrease in tumour multiplicity when compared to controls; however, AP39 and RT01 treatment showed a decrease in gene expression of antioxidant enzymes in tumour tissue. This indicates a reduction in oxidative stress within the tumour microenvironment.

**Conclusions**: AP39 and RT01 could be beneficial when combined with other chemotherapeutic agents and ultimately improve patient outcomes. Mitochondria-targeted $H_2S$ donors could offer a novel treatment option for patients with poor response to current LC treatments.