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Small Probes, Big Impact! Developing Nucleic-Acid based Molecular Probes for Breast Cancer Surgery

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As of 2022, breast cancer is the most diagnosed cancer globally, affecting both men and women, with 2.3 million cases reported annually [1]. Early detection techniques have enhanced clinical outcomes and survival rates. Surgical resection remains the primary curative approach, with approximately 70-90% of affected women undergoing surgery for early-stage disease [2]. During surgery, tumours are meticulously excised with a margin of healthy tissue to ensure complete removal while minimising damage to surrounding tissues. Achieving a negative surgical margin, indicating no residual tumour, is crucial for better long-term survival. However, current intraoperative evaluation techniques, like frozen section analysis, often yield false-negative results, leading to re-operations and increased metastasis risk. Routine immunohistochemistry (IHC) is the gold standard for evaluating surgical margins but takes hours to days, limiting its intraoperative applicability [3,4]. Additionally, commercially available antibodies for IHC often suffer from cross-reactivity and lack specificity, resulting in about 42% of diagnostic inconsistencies [5]. To address these issues, we have developed a nucleic-acid-based probe system using "aptamers" aka chemical antibodies and "DNAzyme" as reporter molecules to complete the intraoperative diagnosis within 30 minutes. Aptamers, being smaller in size, offer faster in vivo diffusion, less steric hindrance, and better tumour penetration for epitope targeting [3,6]. This next generation nonprotein molecular probe system may be small, but it promises big impact by enhancing the accuracy and sensitivity of tumour resection and metastasis diagnosis. This innovation could revolutionise the 130-year-old frozen section pathology procedure, improving the survival and quality of life for breast cancer patients worldwide.

The Pregnancy Research and Translation Ecosystem: Improving the proportion of women meeting the dietary guidelines in pregnancy

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A healthy prenatal diet is important for maternal and child health. Yet over 40% of Australian women do not meet the dietary guidelines. The Pregnancy Research and Translation Ecosystem (PRT-E) is platform for co-design research aiming to implement practical pregnancy care solutions to improve maternal and child health. The clinical stakeholders identified increasing the proportion of pregnant women meeting the dietary guidelines as a research priority requiring immediate action. We aimed to understand clinician perspectives on factors driving poor prenatal dietary intakes, and the current practice around provision of dietary advice in pregnancy care to inform intervention design. We facilitated three online workshops with PRT-E midwives from regional and rural health services in south-western Victoria. Using Group Model Building, we thematically analysed the factors driving poor prenatal diet quality and intervention needs. Our findings indicated a need for time-efficient, cost-effective dietary monitoring solutions that support clinicians to provide high quality dietary advice. IMPACT: These results have been translated into our existing Bugs & Bumps smartphone app, which aims to improve prenatal diet quality. We incorporated an app feature that surveys women's dietary intakes and provides clear, practical dietary advice written by dietitians that can be used by women and their pregnancy care clinicians. Through MRFF funding we are now trailing Bugs & Bumps at Barwon Health, if efficacious we will co-design plans for its incorporation into pregnancy care within PRT-E. Bugs & Bumps has great potential for translation and impact as it directly addresses clinicians' research priorities and needs.

Genetically predicted depression is bidirectionally associated with cardiometabolic diseases: a systematic review and meta-analysis of 35 Mendelian randomisation studies

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Introduction Observational studies have demonstrated that depression is highly comorbid with cardiometabolic diseases. Thus, we can hypothesise that treating depression will reduce cardiometabolic risk. However, clinical trials have rarely demonstrated this, which raises the question if the depression-cardiometabolic disease association is truly causal. Mendelian randomisation (MR) is an emerging analytic technique that uses genetic variants to infer causality between exposures and disease outcomes. Unlike observational studies, MR studies are unaffected by confounding and reverse causality. Therefore, we aimed to synthesise evidence from MR studies to investigate the association between depression and cardiometabolic diseases. Results Forty studies were included in the systematic review, and 35 in meta-analysis. Pooled evidence revealed that depression was associated with coronary artery diseases (OR: 1.11, 95% CI, 1.06 to 1.16), myocardial infarction (OR: 1.17, 95% CI, 1.09 to 1.25), and hypertriglyceridaemia (OR: 1.10, 95% CI, 1.06 to 1.15), and lower odds of high density-lipoproteins (OR: 0.95, 95% CI, 0.91 to 0.99). In reverse MR, obesity (OR: 1.11, 95% CI, 1.05 to 1.18) was associated with higher depression risk. IMPACT These results are suggestive of an independent, likely causal association unaffected by environmental or indirect health behaviours. For my PhD, I will use data from three lifestyle therapy-based trials for depression to further understand under what circumstances depression treatment can improve cardiometabolic risk. This project will have important implications for the health care systems and policy in Australia and beyond, signifying the need for effective health strategies to prevent comorbidities, and alleviate disease burden in high-risk populations.

Potential of Deep Learning Methods in Neuroimaging and Microbiome Data Analysis

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The potential of deep learning (DL) methods in neuroimaging and microbiome data analysis is immense, offering transformative advancements in both fields. DL can enhance the accuracy and efficiency of diagnosing neurological disorders in neuroimaging. Convolutional neural networks (CNNs) have shown promise in identifying structural abnormalities in MRI and CT scans, enabling early detection of conditions such as cognitive impairment and Alzheimer's. DL models can facilitate the analysis of functional MRI (fMRI) data, helping to map brain activity patterns and understand complex neural networks involved in cognitive processes and mental health disorders. DL techniques can handle the high-dimensional and complex nature of microbiome data. Recurrent neural networks (RNNs) and autoencoders are useful for revealing hidden patterns in microbial communities, offering insights into their impact on health and disease. These models help predict microbiome functions, identify disease biomarkers, and support personalized medicine by customizing interventions based on individual microbiome profiles. Our primary goal is to develop predictive models that clarify the Gut-Brain Axis by linking multidimensional microbiome data with brain function markers from fMRI and CAT scans. By merging these datasets, we aim to establish strong correlations between gut microbiota and neurocognitive health, enhancing our understanding and predictive accuracy of neurocognitive disorders. Scalability and adaptability of DL models make them well-suited for handling large-scale datasets, improving the robustness of findings. As computational power continues to grow and new DL architectures emerge, potential for these methods to revolutionize neuroimaging and microbiome research will expand, driving precision medicine and personalized healthcare solutions forward.

Histone Deacetylase and it's involvement in Breast Cancer

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Breast Cancer (BC) has become one of the most prevalent cancers worldwide, with an estimated 2.3 million diagnoses globally each year; 1 in 8 women expected to receive this diagnosis in their lifetime. Breast Cancer is highly heterogeneous with diverse subtypes, requiring different treatments. Investigating BC metabolism is critical for revealing the underlying causes of this variability and identifying viable targets for intervention. Histone Deacetylases (HDACs) are enzymes that remove acetyl groups from histone proteins, affecting gene expression. Previous studies showed an association between HDAC'S and cancer, with HDAC5 emerging as a promising therapeutic target. It has been identified that HDAC5 down-regulates genes associated with oxidative metabolism. However, it remains unclear whether a similar metabolic reprogramming driven by HDAC5 occurs in BC. Utilizing various methods that will measure metabolism and proliferation, we aim to examine HDAC5's role in BC metabolism and protein synthesis in two genetically diverse cell lines, to try and account for the heterogeneity of BC. We hypothesize that a stable knockdown of HDAC5 will enhance oxidative metabolism while decreasing glycolysis, resulting in reduced BC cell proliferation. This has been demonstrated by our preliminary results of one of the cell lines whereby the knockdown of HDAC5 significantly reduced cell proliferation ($p<0.05$). By advancing our understanding of BC metabolism and its relationship to cell proliferation, we aim to uncover novel pathways that can be therapeutically exploited to help treat and or manage this major disease.

Investigating colorectal cancer relapse using a novel zebrafish xenotransplantation model

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Most deaths from cancer are caused by metastasis, the process by which cancers spread in the body. To metastasize, cancer cells that detach from the primary tumour must migrate through tissues, survive inhospitable environments, and evade immune defenses. As such, metastasis can only be studied in vivo, most commonly using mouse models. However, these models have limitations, including the need for sophisticated imaging platforms to track tumour growth in vivo and lack resolution to image the fate of disseminated cancer cells. They are also not amenable for large scale drug screens. Recently, zebrafish have emerged as a useful alternative to mice for studying cancer metastasis. Human cancer cells display similar metastatic propensities when injected into zebrafish and mice, generating tumours with similar pathologies. Zebrafish also allow real time in vivo monitoring of tumor growth and spread and are amenable to high throughput drug screens. In this presentation, I will discuss some of our recent efforts to establish zebrafish models to study cancer metastasis and how we are using these to investigate key problems in the field that remain unresolved, including how some tumour cells survive and thrive in new host tissue environments and the mechanisms underlying cancer relapse.

Creation of a regional data directory – bringing together data resources for the Barwon South West to inform public health action in local communities.

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Background
Navigating existing population health data resources to obtain appropriate information has been identified as challenging by our partners. As part of the Barwon Southwest (BSW) public health strategic actions, we aim to create a population health directory that collates and highlights the scope and strengths of publicly available data resources, which can be used by local government, health and community sector partners.

Methods
Data resources relating to demographics and key population health areas have been identified. Municipal Health and Wellbeing plans from the regions ten LGA's were reviewed and analysed to develop the initial catalogue. Consultations with additional stakeholders will be conducted to inform further inclusions.

Results
The directory includes topic areas such as mental health, physical activity, maternal and child health, smoking and vaping, climate change, and access to services. The directory provides links for accessing publicly available data resources, highlighting strengths and data considerations for each as well as information about the lowest geographic level of data available and demographic breakdowns reported. Data resources identified use a range of data types, including census, population health surveys, administrative data collections, and modelled estimates and projections.

Conclusion
The population health data directory is valuable for supporting BSW ecosystem partners' data needs. The authors are keen to discuss and collaborate with any researchers and organisations to ensure local resources presenting publicly accessible data are captured within this directory. This will enable partners access to comprehensive local data sources to support and optimise effective public health planning, implementation and evaluation regionally.

Investigating colorectal cancer metastasis using a novel zebrafish xenotransplantation model

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Colorectal cancer (CRC) causes over 900,000 deaths each year, primarily due to inability to prevent and treat metastatic forms of the disease. 25% of these patients present with metastasis at the time of initial diagnosis and about half of all CRC patients present with relapse after the treatment. To metastasize, CRC cells leave the primary site and overcome several physiological barriers to successfully colonize distant organs. Standard zebrafish metastasis assays only allow studies on the early stages of metastasis. The fate of the early micro-metastatic lesions observed at 3-day post injection cannot be studied further, as the embryos develop adaptive immune cells (T and NK) cells by 5 days post fertilization, resulting in immune rejection of transplanted cancer cells. Therefore, the actual mechanisms underlying the outgrowth of these micro-metastatic lesions cannot be studied further. To overcome this gap, we establish a novel zebrafish xenotransplantation model, using immune-deficient zebrafish i.e., Casper SCID (Casper il2rgc.a-/-), to elucidate mechanisms facilitating CRC metastatic colonization and to test therapies to block colonization. Casper SCID model facilitates in vivo tracking of the fate of the micromets, enabling investigation of later stages of metastasis. These models offer suitable platform for drug testing as well as allows testing of key target genes that are important in driving tumor growth and progression. Additionally, they may serve as an ideal system for personalized cancer biology by enabling testing of therapeutics on patient-derived tumor samples.