Lay Abstracts

TOBIN

Follicular lymphoma (FL) is an incurable form of Non-Hodgkin Lymphoma with conventional therapies. Although some patients live with the disease for many years, others progress rapidly and experience poor clinical outcomes. Tools which can identify this high-risk group of patients are essential for the development trial that provide individualized therapies. Although current clinical-prediction tools have been developed, none incorporate the anti-tumour immune response.

We have dichotomized the immune response in FL into 'hot' or 'cold' tumours based on the degree of immune cell recruitment. We went on to demonstrate that surrogate markers of this phenomenon identify the subset of patients with rapid progression. In three independent cohorts, 'cold' FL tumours, were associated with a 3-5 fold increase in the number of patients with early progression of disease. This marker outperformed all previous models. These finding suggests that 'cold' tumours are a unique biological entity associated with poor outcomes in FL.

GILLINDER

Defining the clinical phenotype of neuronal autoantibody associated epilepsy.

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Any discoveries in the field of epilepsy, particularly low-risk, low-cost interventions would have considerable personal and economic benefits. Refractory epileptics have limited management options aside from surgery which is risky and not always successful. In the proposed study we will investigate a new subtype of epilepsy associated with antibodies to define its clinical features and evaluate the effectiveness of immune based therapies, which are significantly more cost effective than surgery. This is based on our preliminary study which found specific features that are clinically distinct. Our aim is for these patients to be clinically recognisable as a well-defined subgroup so they can be more easily identified and will therefore receive more appropriate treatment. This will have significant health-cost savings and result in an effective cure for this subgroup of epilepsy, which currently have limited treatment options available.

SISKIND

Reducing the Burden of Cardiometabolic Disease Among People With Schizophrenia

Schizophrenia impacts 1% of the population globally. One third of people with schizophrenia will be refractory to first line treatments, enduring ongoing auditory hallucinations and persecutory delusions. Clozapine, the only antipsychotic licensed for treatment refractory schizophrenia (TRS), can transform the lives of people with TRS. However, clozapine causes obesity and diabetes leading to increased mortality from cardio-metabolic diseases. Research from my group has demonstrated that the diabetes drugs exenatide and metformin can reduce clozapine-associated obesity. Our CODEX trial found people on clozapine lost over 4kg more with exenatide than placebo, while our currently running CoMET trial looks to see whether metformin versus placebo can reduce the initial weight gain among people newly commencing clozapine. If these treatments are effective and implemented they could

improve the quality of life and reduce the mortality gap for the 16,500 Queenslanders living with TRS.

PELOSI

Genetics of Mayer-Rokitansky-Kuster-Hauser syndrome: role of Hnf1b and Wnt5a in Mullerian duct development

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Proper functioning of the female reproductive tract is essential for carrying out a pregnancy and ensure foetal health. Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome is a congenital disorder characterized by the absence of a fully developed uterus. MRKH syndrome affects 1 in 4500 women in the general population and it is found in 10% of women with primary amenorrhea, the absence of menstruation. In addition, more than half of patients with MRKH have additional malformations severely affecting their overall quality of life. To date, the aetiology and pattern of inheritance of MRKH syndrome are completely unexplained. This lack of understanding leads to inadequate diagnosis, counselling, and clinical management of affected women. We have developed a novel diagnostic study to identify genetic variations associated with MRKH syndrome, resulting in the characterisation of novel genes necessary for the correct development of the uterus.

KAPETANOVIC

"OutZincing bacterial pathogens" - Defining zinc-mediated innate immune antimicrobial responses and pathogen evasion strategies

Infectious diseases caused by bacteria are a major threat to human health. To aggravate this, number of pathogens are now frequently resistant to antibiotics, resulting in limited treatment options or treatment failure. My research focuses on uropathogenic *Escherichia coli* (UPEC), the major cause of urinary tract infections. We aim at understanding how our immune cells combat this pathogen and how it can overcome these defence mechanisms. Recently, our team found that macrophages mobilize the zinc to defend against bacterial infections and that, compared to non-pathogenic *E. coli*, UPEC has evolved to survive this immune response. Indeed, it can evade the delivery of zinc by hiding within the macrophage itself, but has also an intrinsic ability to resist zinc toxicity. Taken together, these results show that harnessing zinc may provide some potential avenues to develop treatments to combat UPEC and the diseases it causes, such as urinary tract infections and sepsis.

KARUNAKARAN

A novel therapeutic and diagnostic target to treat and/or predict risk of obesity.

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Obesity is a major public health burden worldwide and is characterized by chronic low-grade inflammation driven by both the immune system and dysregulated metabolism. The gene, RIPK1, is a master regulator of inflammation and cell death pathways. Here, we show that genetic variants near the human RIPK1 gene associate with increased RIPK1 expression in adipose tissue and are strongly linked with the human obesity. Mechanistically, we show that one of these genetic variants controls a transcriptional promotor that increases RIPK1 expression in adipose tissue. Therapeutic silencing of RIPK1 *in vivo* in a mouse model of diet-induced obesity markedly reduces total body weight by promoting anti-inflammatory immune cell retention in the adipose tissue. These findings pave the way for the future application of these genetic variants as a diagnostic tool to predict genetic risk of human obesity, and inhibition of RIPK1 expression as a novel therapeutic to treat obesity.

KUTASOVIC

Breast cancer metastasis to gynaecological organs: a clinico-pathological and molecular profiling study

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We have studied breast cancer patients whose cancer spread to the ovaries and other gynaecological sites. The patients were frequently very young (average 45 years and likely pre-menopausal) and suffered from widespread metastatic disease after variable latency (0-20 years), suggesting they may benefit from extended clinical surveillance. The primary tumours did not express biomarkers typically associated with a bad outcome and many of them had an invasive lobular carcinoma (ILC). They frequently expressed the oestrogen receptor, yet have presumably become resistant to anti-oestrogen therapy. Progression to these sites is likely to be hormonally driven, with tumour cells homing to an oestrogen rich environment, characterised by the maintenance of oestrogen receptor expression in the ovaries. We also identified novel androgen receptor mutations that haven't been described before in metastatic breast cancer. Our work suggests that young age of ILC diagnosis may be a risk factor for gynaecological metastasis.

LIU

Lay Abstract, a short paragraph (150 words, plain text, no figures) explaining the research and its significance in non-technical language.

Iron loading disorders (such as thalassaemia) represent an important class of human disease. As part of the treatment for these diseases, the iron needs to be removed and this is often done using iron-binding drugs known as iron chelators. However, current chelators are not ideal due to side effects or onerous delivery methods. In my current research project, we use a novel type of extremely small particles (nanoparticles) to carry iron chelators to the organs which are at particularly high risk of iron loading. Our studies will provide a new generation of drugs for iron overload diseases that can specifically target the sites of the damage, thereby reducing the chance of side effects. These strategies will greatly improve therapy for patients with both systemic and localized iron overload, and the findings from these studies are expected to have wide application clinically.

SINA

Cancer is one of the leading causes of death in Australia and early diagnosis of cancer can significantly increase the survival rate. However, cancer is not a single disease and due to the large variability in cancer types, there is no universal test available that can detect cancer at an early stage. It is also not feasible to routinely check-up every different cancer types when the diagnosis is complicated, costly and often requires invasive biopsy procedure. We have recently discovered a potential 10-minute universal cancer test that utilizes a unique DNA nano-signature common to all cancers and can detect various cancer types with high specificity and sensitivity. The test has been developed using a novel and minimally invasive approach called interfacial biosensing which utilizes direct interaction of DNA with a bare gold surface to detect cancer. We believe this simple test will potentially revolutionize the current cancer screening system.

WOJCIESZEK

PREGNANCIES AFTER STILLBIRTH: AN URGENT CALL FOR BETTER CARE AND MORE RESEARCH

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There are over two million stillborn babies globally every year. Most parents will conceive again after having a stillborn baby. These parents have an increased risk of stillbirth. The next pregnancy after stillbirth is also a very anxious time for parents, due to constant worry about whether their baby will survive. This was a large, international project to bring together all we currently know about where the gaps in current practice are, and how best to care for parents and their unborn babies in pregnancies after stillbirth. We found parents often receive extra antenatal visits and ultrasound scans in these pregnancies, but parents rarely receive enough emotional support. Critically, the existing scientific studies do not tell us enough about how to prevent stillbirth from happening again. Overall, there is an urgent need for better care and more research to improve the health and wellbeing of families in pregnancies after stillbirth.

TOOSEY-SAIDY

BIOINSPIRED 3D PRINTING FOR PERSONALIZED HEART VALVE TISSUE ENGINEERING

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Valvular heart disease is the worldwide third leading contributor to cardiovascular disease which affects paediatrics and elder patients (70 and above) resulting in more than 5 million deaths annually. Tissue Engineered Heart Valves (TEHVs) aim to overcome the disadvantages of current heart valve prosthesis by providing an alternative mechanically stable valve that also supports tissue growth and remodelling. Additionally, heart valves are characterized to be highly flexible yet tough which are at best only partially replicated in scaffolds for heart valve tissue engineering (HVTE). Thus, improved strategies and fabrication technologies have to be established in order to facilitate their translation from bench to bedside. To address this challenge we have employed a biologically-inspired design and biofabrication strategy aiming to embrace mechanical, structural and geometrical complexities of a native heart valve. Advanced 3d printing techniques allowed for the fabrication of highly tuneable and personalized scaffolds for heart valve tissue engineering providing potential functional living heart valves for paediatric patients.

SUETANI

What is the relationship between physical activity and mental health when you are growing up? : Findings from in the Mater-University of Queensland Study of Pregnancy

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The majority of mental disorders have its onset before age 25. Most people suffering from mental disorders die from chronic physical conditions like diabetes and heart disease. For people with mental disorders, these fatal events tend to occur twenty years earlier than those without.

Because of this, we psychiatrists are becoming increasingly more interested in findings ways of understanding the relationship between potentially life-saving modifiable risk factors like physical activity in young people who are at high risk of developing mental disorders.

In this study, using Queensland data consisting of more than 3000 individuals, we found that physically active status at age 14 did not influence psychological stress level at age 21 but being physically inactive earlier increased the risk of having depression later.

Our findings are important because it shows that being active is not only beneficial for physical wellbeing but also influence future psychological wellbeing in young people.