



**Cancer
Council**
SA

Cancer we
can help.

Beat Cancer Project

Cancer Council's Beat Cancer Project is a collaboration between Cancer Council SA, the State Government, SAHMRI and the Universities. It is the single largest cancer research investment in the state outside of the Federal Government and funds some of the state's best and brightest cancer researchers, enabling them to work towards the next cancer breakthrough.

The following projects are newly funded through Cancer Council's Beat Cancer Project in January 2020, which includes funding from the Commonwealth Medical Research Future Fund. For more information and to view the full list of funded projects visit www.cancersa.org.au/research/beat-cancer-project

2019 Fellowships (across 3 years)

Prof Michael Sorich, Flinders University - \$596,009

Cancer treatment big data: Predicting and understanding patient-specific treatment benefits, harms and prognosis

The research will develop online tools that will help patients to work through difficult decisions about how and when to use an anti-cancer medicine for the treatment of cancer. It will do so by utilising innovative methods to comprehensively analyse a very large amount of data that has recently become available from both clinical studies of medicines and routine use of the medicines by patients. This analysis will allow high-quality predictions to be made regarding a patient's specific likelihood of benefits and harms from using an anti-cancer medicine.

This research will help overcome barriers to the communication of key information and empower patients by providing doctors with a toolkit to present the treatment options and their key outcomes to the patient in a manner that is personalised to their specific circumstances and characteristics. By having this personalised information, patients can feel more confident and empowered to make the most appropriate decision for them specifically regarding their treatment and will be better prepared by having more accurate expectations for their treatment outcomes.

Additionally, the research will provide insight into the patient and disease characteristics influencing benefit and harms from treatment. These insights provide opportunities to better understand why medicines sometimes don't work well for certain individuals and how this may be overcome.

A/Prof Luke Selth, Flinders University - \$597,196

Understanding and overcoming therapy resistance in lethal prostate cancer

More than 350,000 men die from prostate cancer each year worldwide. In Australia, it caused the death of 3,452 Australian men in 2017, and takes more healthy years of life than any cancer except lung. The lethal phase of this disease is referred to as castration-resistant prostate cancer (CRPC), which occurs after failure of hormonal therapies (“androgen deprivation therapies”). CRPC is currently treated with new and more potent androgen deprivation therapies and chemotherapy, but the survival benefits associated with these treatments are in the order of months and all can cause severe side-effects in patients. In short, better treatments for CRPC are urgently required, a reality strongly endorsed by our team’s consumer advocates, all of whom are prostate cancer survivors.

My vision over the next 3-5 years is to use the latest technological advancements in cancer research to better understand how lethal prostate cancers grow, and then use this information to discover new therapeutic strategies. My longer-term goal is to develop new drugs that will have a major impact on reducing death caused by prostate cancer.

Dr Ilaria Stefania Pagani, SAHMRI - \$300,000

Identifying and exploiting metabolic dependencies for improved therapeutic outcomes in chronic myeloid leukaemia patients

Chronic myeloid leukaemia (CML) can be controlled by tyrosine kinase inhibitors (TKIs), but about 20% of patients are resistant to first-line therapy and some of them develop fatal blast crisis. Even when treatment is effective most patients need to take TKIs lifelong. This means that there are now thousands of Australians dependent on TKIs, with resulting side effects and costs. Persistent disease indicates the failure of TKIs to target the CML stem cells. Stem cells have a unique metabolic profile characterised by energy production through the mitochondria. Giving a TKI together with a drug that blocks stem cell metabolism could eradicate persistent cells and contribute to an eventual cure. Mitochondria possess their independent DNA (mtDNA), that is more susceptible to mutations than nuclear DNA. In a preliminary study we showed for the first time that more mutations in mtDNA are associated to a better outcome in CML patients. MtDNA mutations could affect the function of the mitochondrion, increasing its susceptibility to undergo apoptosis in response to TKI therapy. Therefore, stem cells from good responder patients could rely more on glycolysis for their survival. To the contrary, stem cells from poor responder patients, with intact mitochondria, could rely to a different metabolism, for example being more dependent on mitochondrial respiration. The re-purpose of existing drugs targeting metabolic vulnerabilities represents a significant breakthrough in precision medicine and may lead to a rapid translation into clinical practice.

Dr Stephanie Reuter Lange, University of South Australia - \$300,000

Optimising cancer therapy through development of evidence-based dose individualisation strategies

Whilst there has been substantial improvements in the treatment of cancer, it remains that 3 out of 10 patients will not survive longer than 5 years, a result of either cancer progression or death from severe treatment-related side effects. Cancer medicines must be administered at a dose that is enough to treat the cancer, but not too much to cause toxic side effects. While this is well known, most cancer treatments are given as a “one-size-fits-all” amount. Given the large variability in response seen with many cancer medicines, this means that for the same dose some patients are likely to be under-treated and others a likely to be over-treated. The concept of dose individualisation is tailoring the amount of drug administered to each individual patient to maximise tumour response and minimise side effects. This fellowship program will use computer-based modelling methods to identify dose individualisation strategies for best treatment practice. This will be conducted for a range of diverse projects that will illustrate the value in this approach to cancer treatment and provide a framework for determining the best use of new and existing cancer medicines.

Dr Madelé van Dyk, Flinders University - \$240,000

Evaluating the capacity and benefit of precision medicine strategies to account for inter-patient variability with anti-cancer drugs used for advanced cancers

Since the discovery of kinase inhibitors (KIs), a class of targeted therapy against terminal cancers, progression-free survival and overall survival has greatly improved. However, KIs undergo complex metabolism via liver enzymes (CYP3A4), which is known for its substantial variability in activity. However, no marker to identify CYP3A4 activity in patients currently exists. Due to the wide inter-individual variability, KI concentrations have varied over 10-fold. Despite knowing this, variability between patients are inadequately addressed and a 'one-size fits all' prescribing is used. This clinical issue is widely recognised but still we do not account for this variability, resulting in some patients experiencing therapeutic failure or toxicity because the dose is not enough or too much.

Therapeutic drug monitoring (TDM) can address this, measuring drug concentrations and changing the dose until the patient's concentration is in the 'target concentration'. Based on my previous work I have shown that with the implementation of TDM, we can prolong progression-free survival significantly and thus improve patient quality of life. I have also shown that patient characteristics can be used to account for this inter-individual variability. Therefore, this study will evaluate the capacity and benefit of TDM to optimise KI dosing and determine which patient characteristics can help to predict a better dose so that we can personalise treatment to each individual and maximising treatment and minimising side effects. Since the economic health benefit has never been evaluated, this study will be the first to address this by performing a cost-benefit analysis.

Dr Krzysztof Mrozik, The University of Adelaide - \$240,000

Novel drug delivery approaches to improve the quality of life and survival of patients with multiple myeloma

Multiple myeloma (MM) is an inoperable blood cancer that grows within bones. Drug therapy is integral to the treatment of patients with MM; however, it frequently results in debilitating side effects, negatively impacting quality of life. For instance, while the standard-of-care MM drug bortezomib (VELCADE®) is effective at treating the cancer, many patients are plagued by peripheral neuropathy, a painful and highly debilitating nerve condition affecting the hands and feet. This condition frequently necessitates dose reduction or even treatment cessation, which adversely affects patient survival.

One approach to minimise the risk of drug side effects is to improve drug delivery to sites of tumour. In this project, I will investigate novel approaches to selectively increase the delivery of commonly used MM drugs to sites of MM tumour, and the utility of these approaches to effectively treat the cancer and reduce drug side effects will be assessed. Firstly, I will utilise agents that transiently disrupt tumour vasculature, enabling the selective enhancement of drug delivery to sites of MM tumour and thereby an increase in effectiveness of low doses of drugs. Secondly, I will utilise state-of-the-art nanoparticles to selectively deliver drugs to sites of MM tumour, thereby minimising the exposure of normal tissues to drugs. Ultimately, this project has the potential to reduce the incidence and severity of drug side effects, leading to significantly improved quality of life and survivorship in many patients with MM.

Research Project Awards for 2020

Dr Craig Wallington-Beddoe, Flinders University - \$100,000

Investigating Desmoglein-2 as a superior biomarker and therapeutic target for multiple myeloma

Multiple myeloma (MM) is an incurable aggressive cancer of the bone marrow. In Australia, 1,876 new cases were diagnosed in 2018 with an estimated five year survival rate of 50% and treatment costs exceeding \$700,000 per patient. We have identified desmoglein-2 (DSG2), a cell surface protein, to be elevated in 35% of MM patients who are three times more likely to die within six years of diagnosis. This study examines a new prognostic tool to rapidly identify these patients and new DSG2-targeting therapies.

Dr Iain Comerford, The University of Adelaide - \$100,000

Improving T cell homing to solid tumours

This project aims to identify and test the role of novel molecules in controlling movement of cells of the immune system into solid tumours. Many cancers survive by preventing immune cells that are capable of killing cancer cells from entering the tumour mass. This project takes innovative new approaches to identify molecules that control this process. In addition, we have already identified a molecule involved in this process and will test how this limits immune cell entry into tumours.

Prof Peter Hoffmann, University of South Australia - \$100,000

Defining a molecular signature for endometrial cancer staging

Metastasis is the primary cause of death from solid cancers especially in endometrial cancer. In most patients it is impossible to know without radical surgery who is suffering from metastasis. This project will develop a diagnostic method utilizing latest mass spectrometry technology to determine these patients. The new diagnostic method will save lives and spare patients unnecessary interventions which are associated with significant morbidity and loss of quality of life.

Prof Timothy Hughes, The University of Adelaide - \$100,000

Developing an artificial intelligence-based algorithm to enable a risk-adapted approach to frontline therapy in chronic myeloid leukaemia (CML)

Even with our current choice of five drugs, around 20% of patients with chronic myeloid leukaemia (CML) respond poorly to standard drug therapy. We plan to develop an algorithm based on the most predictive biological and molecular assays to enable a "precision medicine" approach to CML therapy. This "risk-adapted" approach would direct most patients to the safest and cheapest therapy whereas "high risk" patients would receive more potent therapy or enter a trial of combination therapy.

Prof Caroline Miller, The University of Adelaide - \$100,000

Artificially-sweetened beverages, fruit juice and water consumption: the unresolved substitution effects from sugar-sweetened beverage policy

Sugary beverages contribute excess energy to the diet, cause tooth decay, obesity and diabetes. Reducing excess consumption is an international public health policy priority. However, the effects of these policies in terms of substitution with other beverages are largely unknown. This study will investigate consumers' substitution of water, artificially-sweetened beverages and fruit juice for sugary drinks, and make recommendations for public health policy.

Dr Luke Selth, The University of Adelaide - \$100,000

Targeting microRNA-regulated tumour plasticity to improve prostate cancer outcomes

The development of therapy resistance in prostate cancer kills >3,000 men per year in Australia. Recent work from our team has identified a factor, miR-194, which promotes therapy resistance and the growth of lethal prostate cancer. In this study, we will determine how miR-194 does this, and test whether targeting miR-194 could be a useful therapeutic strategy to improve patient outcomes.

Beat Cancer Infrastructure Award

Prof Kim Moretti, SALHN - \$75,000

Prostate cancer in South Australia - Moving the clinical registry forward

Prostate Cancer is the most common non-skin cancer of men in Australia. The disease can be treated in many different ways including surgery, radiation therapy, hormone treatments and chemotherapy. This infrastructure funding will support a registry capturing all men diagnosed with prostate cancer in South Australia and record their clinical and treatment details. This information can be used to benchmark the standard of care delivered in the state and also enable research projects.

Cancer Council SA

ABN: 31 469 615 538

Cancer Council SA is the business name of the Anti-Cancer Foundation of South Australia

South Australia

202 Greenhill Road
Eastwood SA 5063

PO Box 929, Unley BC SA 5061

t 08 8291 4111

f 08 8291 4122

e cc@cancersa.org.au

13 11 20

Every minute. Every hour. Every day.
cancersa.org.au