ACRF
ACCELERATE
An Impact Philanthropy Initiative

AUSTRALIAN CANCER RESEARCH FOUNDATION

Developing tailored patient treatment approaches in real-time

Project Title	ACRF Centre for Advanced Cancer Modelling
Lead Institute	Macquarie University, Sydney
Focus Area	Precision Oncology, Targeted Therapies
Cancer Types	All solid tumours including rare cancers – the initial focus will be melanoma, head and neck, glioblastoma, urogenital, and non-small cell lung cancer

Challenge and Opportunity

Despite the remarkable effectiveness of targeted therapies many patients still die of cancer. Biomarker based precision oncology helps assess the best treatment for an individual by looking for the unique pattern of genes, proteins, and other substances (called biomarkers) that can provide information about a person's cancer. This has delivered many successes but has not produced long lasting benefits for patients. There is a need to integrate new approaches to identify and assign existing and new drugs to cancer patients who will respond.

The ACRF Centre for Advanced Cancer Modelling (ACRF CACM) will bring together clinical, research and bioengineering expertise to advance the development of cancer tissue models to inform treatment decisions. These models will deliver new insights into mechanisms of drug resistance across a range of cancers, providing information as to what drives a protective memory for immunotherapy and potentially identify new drugs. These dynamic disease models will be integrated into clinical care to transform the management of cancer patients and provide new avenues for personalised treatments.

"This ACRF grant is an important catalyst that will expand our research expertise & capabilities by providing access to state-of-the-art equipment & cutting-edge facilities."

Professor Helen Rizos Chief Investigator ACRF CACM

Project in Brief

- It is not yet clearly understood why precision oncology (in which genomic profiling of a cancer is used to tailor treatment) is not effective for everyone or does not lead to long-lasting effects.
- The ACRF Centre for Advanced Cancer Modelling will deliver new knowledge on the mechanisms of resistance to molecular and immune-based therapies in a broad range of cancers. It will also provide insights into protective memory and reveal novel therapeutic targets that can circumvent treatment resistance.
- The ACRF Centre for Advanced Cancer Modelling will provide a world-class, comprehensive precision oncology platform to develop and integrate functional cancer models into clinical decision making and translational cancer research.
- The Centre will significantly enhance the strong research partnerships within the Melanoma Institute Australia and the Chris O'Brien Lifehouse, and will harness new research collaborations nationwide. It will serve as a hub to support the development of early-career and mid-career researchers via mentoring and education programs.

Project Detail

Introduction

Precision oncology, in which tumours are profiled to identify alterations that can be targeted, is a rapidly developing area of medicine and over the last decade has revolutionised cancer care. Two types of treatment that are often used in precision oncology are: immunotherapy (which uses the body's immune system to fight cancer), and targeted therapies (drugs designed to attack a particular target on a cancer cell). Immune checkpoint inhibitors, the most widely used type of immunotherapy, is now an option for nearly 50% of patients with advanced cancer[1,2]. And there are over 30 approved targeted therapies for a range of cancers including melanoma, chronic myeloid leukaemia, breast, colorectal, gastrointestinal, and non-small cell lung cancer[3]. Despite the remarkable effectiveness of these treatments many patients still die of cancer. To fully optimise the potential of these transformational therapies, approaches to identify and assign existing and new drugs to patients that will be responsive are needed.

A Unique Approach

The ACRF Centre for Advanced Cancer Modelling offers a new approach. Using a suite of novel technologies, the ACRF Centre for Advanced Cancer Modelling will develop and integrate functional cancer models into clinical decision making. Using tissue, cellular and liquid models of cancer, the way in which treatments are selected and patients are managed will be transformed. These models will enable the dynamic evaluation of treatment responses and provide insights into mechanisms that underly treatment and resistance. Ultimately, they will support clinical decision making in real time - an important distinction from other international initiatives that are developing cancer models. The Centre brings together a unique capability which builds on existing partnerships and collaborations, to advance the development and utility of these cancer models.

The Centre will expand the growing research capacity at Macquarie University, enabling new capabilities, and building new collaborative research programs. At the broader national level, it will act as a catalyst for advancing cancer research and clinical translation, establishing strategic partnerships, and providing access to shared technology resources.

Research Program

The ACRF Centre for Advanced Cancer Modelling will address three central themes:

1. The development of personalised cancer models to test drug responses and inform tailored treatment decisions

Patient-derived models have the potential to improve the success of personalised treatment approaches. In the ACRF Centre for Advanced Cancer Modelling, tumour tissues from cancer patients will have multiple available therapies applied and responses about drug efficacy will be provided in real time. These models will be embedded in clinical trials and, alongside other data, will be used to guide the selection of treatments. A particular focus will be the creation of models from people with rare cancers and cancers with poor prognosis, to validate potential treatments.

2. Examining treatment resistance and restoring treatment response

Mouse cancer models for melanoma, glioblastoma and breast cancer developed by the research team will be utilised to identify mechanisms of treatment resistance. It is known that the immunotherapy response in individual patients is dominated by a small number of immune cells that expand on treatment and persist over several years[4,5,6]. This ‘protective memory’ has been demonstrated by members of the research team in a melanoma mouse model[7]. The role of the protective memory in generating a durable response to immunotherapy will be investigated in cancer patients – specifically the characterisation of small vesicles generated by immunotherapy. In addition, mechanisms that create a vulnerability in cancer cells leading to resistance to immunotherapy will be further investigated and strategies to restore this tested.

3. The discovery and application of liquid biopsy biomarkers to enable real-time monitoring of patient treatment responses

Liquid biopsies allow for the analysis of tumours using biomarkers circulating in fluids and provide an exciting opportunity to deliver personalised cancer care. Circulating biomarkers allow the characterisation of all tumours when they have metastasised (i.e. spread from the organ where the cancer started) in real-time and are easily repeatable over time. Focussing on melanoma and Non-Small Cell Lung Cancer patients at early stages who have been treated with adjuvant (i.e. post-surgery) chemotherapy/immunotherapy and patients at advanced stages who receive palliative immunotherapies. This will identify liquid biomarker signatures that can determine patients who require and respond to adjuvant therapy and patients who respond to palliative immunotherapies.

The Benefit

The advances resulting from the ACRF Centre for Advanced Cancer Modelling will lead to a greater understanding of treatment resistance in a broad range of cancers and reveal novel therapeutic targets and biomarkers to improve patient outcomes. The development of tissue models from cancer patients will enable the testing and monitoring of treatments in real time. This will result in matching of treatments to patients most likely to benefit, expedite the development of new therapies and limit patient exposure to potentially ineffective drugs. Ultimately this will increase survival and, by reducing adverse effects, improve quality of life for cancer survivors.

Use of Funds

The $2 million investment will support the development of the ACRF Centre for Advanced Cancer Modelling. This will provide the novel technologies and associated support to transform the personalised treatment of cancer patients.

<table>
<tr><th>Technology</th><th>Cost</th></tr>
<tr><td>BIO CellX bioprinter</td><td>$145,000</td></tr>
<tr><td>Molecular Devices ImageXpress Micro Imaging System</td><td>$631,990</td></tr>
<tr><td>Miltenyi MACSima Imaging platform</td><td rowspan="2">$923,010</td></tr>
<tr><td>Miltenyi Biotec UltraMicroscope Blaze</td></tr>
<tr><td>Research Officer</td><td>$300,000</td></tr>
<tr><td>Total</td><td>$2,000,000</td></tr>
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Cancer research lab at Macquarie University in Sydney

Meet the Team

The ACRF Centre for Advanced Cancer Modelling includes a team of 10 Chief Investigators (listed below) and 23 scientists and research specialists. This brings together a diverse team of experts in the clinical management of melanoma, non-small cell lung cancer, head and neck cancers, glioblastoma and urogenital cancers and internationally recognised researchers in liquid biopsy research with unique expertise in 3D cancer models and nanoparticle design.

Chief Investigator Helen Rizos
Head, Precision Cancer Therapy Laboratory, Professor, Cancer Research, Macquarie University Chair, Melanoma Institute Australia Research Committee

Chief Investigator Howard Gurney
Director, Clinical Trials, Macquarie University
Head, Cancer Program, MQ Health, Macquarie University Senior Staff Specialist, Medical Oncology, Westmead Hospital

Chief Investigator Elena Shklovskaya
Senior Lecturer, Macquarie University

Chief Investigator Georgina Long AO
Co-Medical Director, Melanoma Institute Australia, University of Sydney
Chair of Melanoma Medical Oncology and Translational Research Melanoma Institute Australia and Royal North Shore Hospital, The University of Sydney

Chief Investigator Jenny Lee
NHMRC Emerging Leader Fellow, Macquarie University
Visiting Medical Officer, Specialist (Medical Oncology) Chris O'Brien Lifehouse

Chief Investigator Yuling Wang
Future Fellow Professor in Chemistry, Macquarie University
Chief Investigator Antonio Di Ieva. Professor of Neurosurgery, Macquarie University
Professor of Neurosurgery, Italian Ministry of Education, Universities and Research
Associate Professor of Neuroanatomy, Medical University of Vienna, Austria

Chief Investigator Anna Guller
Biotechnologist & Experimental Pathologist Macquarie University Research Fellow, Macquarie University

Chief Investigator Jonathan Clarke AM
Lang Walker Family Foundation Chair and Conjoint Professor in Head and Neck Cancer Reconstructive Surgery, Sydney Medical School, Faculty of Medicine and Health, The University of Sydney and Chris O'Brien Lifehouse.

Chief Investigator Ruta Gupta
Clinical Director of the Department of Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital. Lead Pathologist of Head and Neck Oncology and Thyroid Multidisciplinary Team, Chris O'Brien Lifehouse.

ACRF Model for Impact

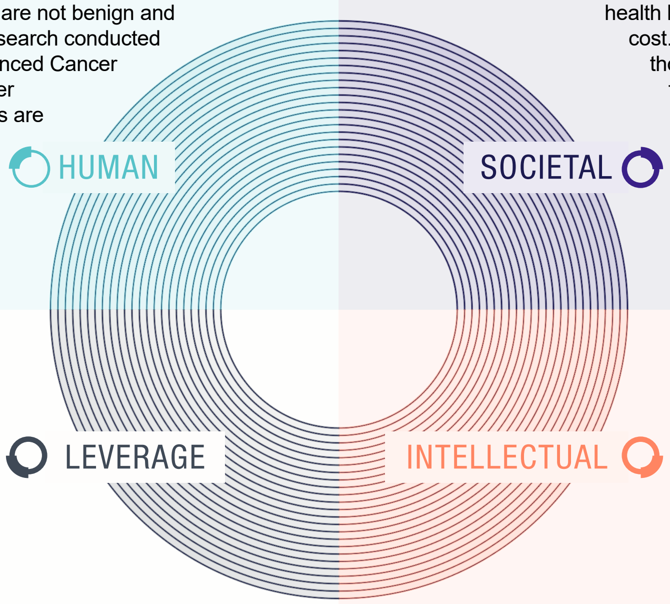
With input from health economic specialists, ACRF has developed a framework to articulate the anticipated future impact of projects that receive ACRF funding. Below is an overview of the outcomes the ACRF Centre for Advanced Cancer Modelling has the potential to achieve:

HUMAN

- In 2023 it is estimated that 165,000 Australians will be diagnosed with cancer and 51,000 will die. Precision oncology treatments, such as immunotherapies, have the potential to benefit over 8,000 Australians[8]. Greater accuracy in identifying precision oncology treatments that will benefit patients would greatly increase this number.
- Immune and molecular therapies are increasingly used in early-stage cancer treatment however not all people respond[9,10]. These therapies are not benign and can impact quality of life. Research conducted in the ACRF Centre for Advanced Cancer Modelling will result in a better understanding of which drugs are most effective and will positively benefits patients.

SOCIETAL

- The ACRF Centre for Advanced Cancer Modelling has the potential to reduce the burden on caregivers who, when considering time spent caregiving for loved ones, work absenteeism and presenteeism, experience a 23% work productivity loss because of caregiving[12,13]. Based on the average Australian wage, this accounts for an annual productivity loss of $13,916 per caregiver annually.
- A precision oncology approach can deliver health benefits at a potentially affordable cost. The use of a test that can select those patients who can benefit from a particular treatment or monitor the therapeutic response during the early stage of the development of precision oncology drugs has been found to reduce the cost of development by $US1.1Bn[14].



LEVERAGE

- Over the last five years the research team have secured over $43M in competitive grant funding. The investment in the ACRF Centre for Advanced Cancer Modelling would significantly strengthen future grant applications and secure additional funding.
- Of the $78B net present gains generated by medical research from 1990 to 2004, $52B was in the form of health gains and $26B in wider economic gains[11]. Extrapolating these figures, the $2M invested by the ACRF has a potential return of $5.23M - $7.8M in the form of health gains and $2.57M in the form of wider economic gains.
- Additional funding of $1.1M will be provided by Macquarie University to sort the Centre. A further $500,000 will be provided by the Cancer Institute NSW to support a research specialist with experience in genomics and bioinformatics.

INTELLECTUAL

- Jobs in medical research are high value and knowledge-based jobs that contribute substantially to the economy. The core team alone (excluding the CI's) has the potential to generate $804,000 in value added gain[11].
- One of the most important outputs of the ACRF Centre for Advanced Cancer Modelling will be publications to inform future research. The $2M invested by ACRF alone has a potential return of 23 publications[15].

For references, please visit acrf.com.au/philanthropy-accelerate-references

BACKING BRILLIANT

AUSTRALIAN CANCER RESEARCH FOUNDATION

Contact Information

To find out more about ACRF Accelerate and this exciting project please contact:
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