

Uncovering biological insights in the tumour microenvironment

Project Title	The ACRF Centre for Mass spectrometry Analysis of Tumour Response In compleX microenvironments (The ACRF MATRIX Centre)
Lead Institute	Garvan Institute of Medical Research, NSW
Focus Area	Harnessing the power of spatial proteomics to uncover why some cancers resist treatment and spread
Cancer Types	Pancreatic, breast, prostate, and lung cancers with implications for all solid tumours



The ACRF MATRIX Centre seeks to revolutionise our ability to investigate why some cancers resist treatment and spread to other organs. Whilst most cancer research focuses on tumour cells themselves, we're investigating the 'neighbourhood' the cancer cells live in – "the tumour microenvironment".

*Dr Amelia Parker and Professor Thomas Cox,
 Chief Investigators*

Challenge and Opportunity

Cancer treatment outcomes are often undermined by two critical challenges:

- 1. Therapy resistance** driven by dynamic changes in the tumour microenvironment both during and following treatment.
- 2. Metastatic spread to secondary sites** that do not respond in the same way as primary tumours due to differences in host tissue.

Despite significant advances in cancer treatments, we still do not fully understand how they work at a biological level, or how cancers sometimes manage to survive and resist treatment. In particular, our understanding of the surrounding environment in which tumours grow is immature. This gap in knowledge limits our ability to fully explain treatment responses and to develop better therapies.

A tumour does not exist on its own — it lives within a complex neighbourhood made up of supporting cells, immune cells, and structural tissues. Cancer cells interact with this ecosystem, and interactions strongly influence how tumours grow, spread, and respond to therapy. How this environment changes over time, how it reacts to therapy, and how it differs between original tumours and those that spread to other parts of the body are important but not well-studied areas of cancer research. To uncover potential vulnerabilities in this tumour microenvironment, we need advanced research technologies and a systemic, multifaceted approach.

Project in Brief

Through establishing world-leading Australian capability in spatial proteomics mass spectrometry imaging, the ACRF MATRIX Centre aims to reveal how tumour microenvironments evolve during therapy and drive metastatic spread, identifying novel biomarkers and therapeutic targets currently invisible to genomic approaches (DNA sequencing). This national infrastructure will also train and skill early and mid-career researchers across Australia.

Using cutting-edge mass spectrometry imaging technology, researchers will be able to visualise how the tumour microenvironment changes during patient treatment - particularly in samples from patients receiving chemotherapy or immunotherapy.

This will allow researchers to identify why some tumours become resistant and others respond. The team will also map the molecular differences between primary tumours and metastatic lesions in different organs, revealing why secondary cancers often behave so differently from the original tumour. These discoveries will help drive the development of new combination therapies.

The flagship projects will focus on pancreatic, breast, prostate, and lung cancers, chosen because of the existing exceptional clinical cohorts. Discoveries will likely inform researchers working in all solid tumours. Importantly, this technology is highly suited to analysing archival patient tumour material, opening up the potential for researchers to study any solid cancer type.

Spatial proteomics is the study of where proteins are located in cells and how their positions affect what they do.



A biomarker is a naturally occurring molecule, gene, or characteristic by which a particular pathological or physiological process, disease, etc. can be identified.

Mass spectrometry is used in cancer research to find, measure, and compare molecules that are different in cancer cells versus healthy cells. Because it can detect very small changes - it's especially powerful for early detection and understanding how cancer behaves.

The Benefit

By revealing why tumours resist treatment and how they establish metastatic colonies in distant organs, this research will enable researchers and clinicians to design smarter combination therapies that target both cancer cells and their supporting microenvironment simultaneously. Additionally, researchers will be able to identify biomarkers that predict which patients will respond to specific treatments, sparing non-responders from ineffective therapies and their side effects.

Fundamental biological insights often follow technological breakthroughs. The spatial 'omics' technology of the ACRF MATRIX Centre will break through the barrier that has kept the tumour microenvironment largely invisible to genomic approaches, whilst establishing national infrastructure that can accelerate discoveries across the entire Australian cancer research community.



Bruker timsTOF fleX MALDI-2 Mass Spectrometer



“Most cancer therapies target the cancer cells themselves. And what we’re now realizing is it’s actually the tissue around the cancer cells that’s remodelling and changing as tumors progress. And it’s that remodelling that actually influences whether a tumor will respond to treatment or not.”

Professor Thomas Cox, Chief Investigator

Use of Funds

The \$2.5 million investment will enable purchase of a Bruker timsTOF fleX MALDI-2 system. This new technology enables comprehensive molecular profiling of proteins, lipids, metabolites and drugs simultaneously at single-cell resolution across entire tumours. With up to 100-fold greater sensitivity than conventional approaches, it can reveal low-abundance molecules that previous technologies couldn’t detect, enabling unbiased discovery of unexpected players in therapy resistance and metastasis.

Technology	Cost
Bruker timsTOF fleX MALDI-2 Mass Spectrometer	\$2,500,000
Total	\$2,500,000

Meet the Team of Chief Investigators



Lead: Professor Thomas R. Cox, BSc (Hons), PhD
Laboratory Head - Matrix & Metastasis, Garvan Institute

Professor Alexander Swarbrick, BSc, PhD
Co-Director of the Cancer Ecosystems Program
Laboratory Head - Tumour Progression, Garvan Institute

Professor Marina Pajic, BSc, MSc (Hons), PhD
Co-Director of the Translational Oncology Program
Laboratory Head - Personalised Cancer Therapeutics, Garvan Institute

Dr Amelia Parker, BEIBSc, PhD
Senior Research Officer, Garvan Institute

Professor Paul Timpson, BSc (Hons 1), PhD
Co-Director of the ACRF INCITe Centre
Co-Director of the Cancer Ecosystems Program
Laboratory Head - Invasion & Metastasis, Garvan Institute

Professor Sarah Kummerfeld, BSc (Hons 1), PhD
Chief Scientific Officer and Head of Data Science, Garvan Institute

Professor Sandra O'Toole, BMedSci (Hons 1), MBBS, FRCPATH, PhD
Senior Staff Specialist, tissue pathology and diagnostic oncology, RPAH
Senior pathologist, Garvan

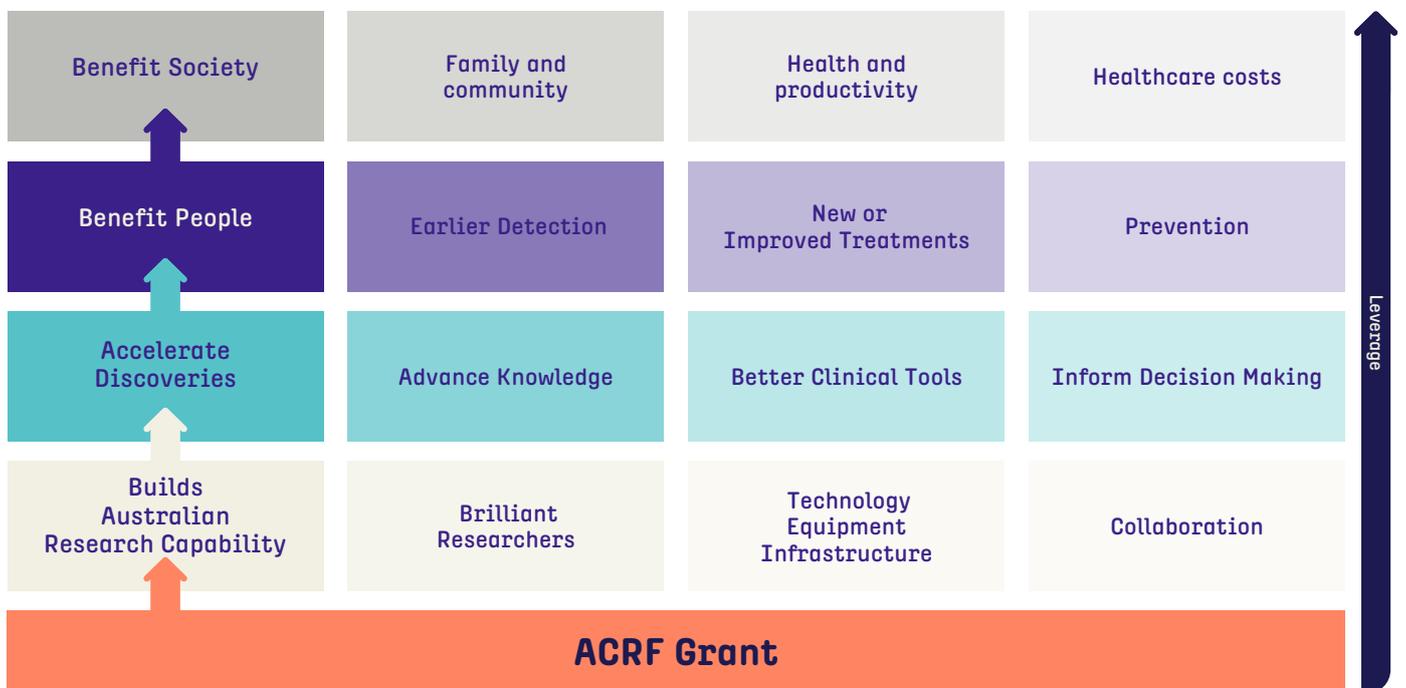
Professor Lisa Horvath, MBBS (Hons 1), FRACP, PhD
Chief Clinical Officer & Director of Research
Conjoint Chair of Medical Oncology, Chris O'Brien Lifehouse
Head of Advanced Prostate Cancer research group, Garvan Institute

Professor Lorraine Chantrill, BSc/M.B.B.S, FRACP, PhD
Senior Staff Specialist Medical Oncologist, Co-Director for Medical Oncology and Area Director of Clinical Trials for the Illawarra Shoalhaven Local Health District
Senior Staff Specialist Medical Oncologist, The Kinghorn Cancer Centre (Garvan Institute) and Conjoint Clinical Lecturer, University of Western Sydney

Dr Rachel Galimidi, BSc 2005, PhD
Head of Development Platform and Head of Biologics Platform, Garvan Institute

ACRF's approach accelerates impact

- ACRF is uniquely positioned to access brilliant researchers and facilitate collaboration across Australia. Our focus on equipping researchers with technology and infrastructure is vital to progress and innovation.
- An outstanding independent panel of Australian and international cancer experts recommended funding this project. The research is cutting edge, distinctive, and has the potential for impactful outcomes.
- Projects outcomes will be reported to ACRF for seven years. These typically include scientific breakthroughs, advanced knowledge, publications, new approaches both in the clinic and use of information.
- The impact for people affected by cancer – through earlier detection, new and improved treatments – is better quality of life through the diagnosis, and lives saved. In some cases, research even results in preventing cancer.
- Furthermore, research benefits society – including keeping families and communities intact, reducing healthcare costs and keeping people healthy and productive.



ACRF seed funds remarkable projects and recipients typically leverage the ACRF grant to secure funding from other funding agencies. Reports from 33 grants (2013 – 2023) with an award total of \$80 million evidence self-reported leverage to \$778 million, a factor of 9.6 times.

Beyond the primary research objectives ACRF funded equipment has been used in the training of numerous new doctors and scientists, and it has played a part in attracting and retaining leading talent in Australia and global acknowledgement of the high quality of Australian cancer research.

**B A C K I N G
B R I L L I A N T**

To find out more about Australian Cancer Research Foundation, the ACRF Accelerate program and this exciting project please contact philanthropy@acrf.com.au **1300 884 988**