

# Reducing childhood cancer deaths through better understanding of predisposition

<b>Project Title</b>	The ACRF Childhood Cancer Early Detection, Prevention and Treatment Program
<b>Lead Institute</b>	Children's Cancer Institute, Sydney
<b>Focus Area</b>	Targeting previously untreatable cancers and identifying children at risk of getting cancer
<b>Cancer Types</b>	Childhood cancers

## Challenge and Opportunity

Cancer remains the leading cause of death by disease in children less than fourteen years of age. Cancer in children makes up ~3% of the global incidence of cancer, translating to ~1,000 new cases/year in Australia. Sadly, paediatric cancer has a disproportionate impact - beyond the physical and emotional toll on children, their families and the community - the number of years of productive life lost to childhood cancer is proportionately higher than that of adult disease.

While overall survival rates for childhood cancer have improved dramatically over the last few decades, the prognosis for some childhood cancers (including brain tumours, soft tissue sarcomas and neuroblastomas) remains bleak. Those who do survive, face lifelong adverse health effects due to first-line treatment (surgery, chemotherapy, radiation), with at least 60% of young adults developing chronic health conditions, and by the age of 45, 80% experiencing at least one serious disabling or life-threatening condition.

While survival rates for many childhood cancers have improved dramatically, the prognosis for some cancers (including brain and soft tissue) is still poor.

**“ACCEPT’s research will lead to faster discoveries, more successful treatments, and a broader global shift towards personalised, precise, and preventative cancer care, improving outcomes for all cancer patients in the future.”**

***Professor Glenn Marshall AM, Chief Investigator***



“The exciting thing about this program is its integration with ZERO - this makes it more than just a research program to understand cancer. It means that whatever we find can really quickly be applied to every child with cancer in the country. And so that turnaround means that this is not just research, but this is actually making a difference.”

*Professor Michelle Haber AM, Chief Investigator*



Australian Cancer Research Foundation (ACRF) has provided three previous grants to initiate and support Children's Cancer Institute (CCI) world-leading and internationally unique national precision medicine program that is inclusive of all children through all stages of the cancer journey. Combining this program with accumulated learnings from decades of pioneering translational research gives unprecedented opportunity to address the most critical remaining challenges in childhood cancer:

1. How to better diagnose childhood cancer predisposition and prevent early disease progression?
2. How to treat patients more effectively to prevent disease recurrence?
3. How to address the urgent need for drugs targeting currently undruggable child cancer targets?

## TECH TALK

### Unravelling childhood cancer genetics

It is necessary to unravel the complete genetic repertoire of paediatric malignancies, which differ substantially from adult malignancies in terms of their histopathological and molecular subtypes. Over the last nine years, researchers at CCI have generated a vast wealth of previously unobtainable data and matched tumour/normal biospecimens from high-risk child cancer patients through the Zero Childhood Cancer Program (ZERO), a national precision medicine program.

These resources have enabled researchers to identify new aspects of the unique genetic and epigenetic landscape of high-risk childhood cancer, leading to new hypotheses pertaining to disease origin, development, and progression, and revealing novel treatment opportunities.

From December 2023, the Zero Childhood Cancer Program (ZERO), a national precision medicine program, expanded to include all Australian children with cancer, irrespective of their cancer type or level of risk, making Australia the first country globally to provide access to precision medicine for every child with cancer.

This has provided access to patients with earlier stages of disease (or indeed those who carried a risk of cancer predisposition) providing new opportunity to validate and translate these hypotheses into clinical impact through the prevention of disease, and of disease progression. However, the team lack the firepower to progress these pioneering lines of investigation expeditiously, concurrently and at scale.

## Project in Brief

The ACRF Childhood Cancer Early Detection, Prevention and Treatment (ACCEPT) program will build on the success of the existing Zero Childhood Cancer Program (ZERO). It will provide the infrastructure to translate new data into clinical impact and patient benefit, targeting previously untreatable cancers and better identifying children at risk of getting cancer. It will combine computational biology, high-throughput-compatible and physiologically relevant preclinical platforms, multifaceted functional assays, and scalable robotics to:

- Diagnose cancer predisposition, preventing early progression and recurrence
- Research safer and more effective treatments
- Develop targeted therapies for previously untreatable cancers

### The ACCEPT Program has three main objectives:

#### EXPAND

Expand our understanding of paediatric cancer predisposition and early development, with a view to developing diagnostic tests for cancer predisposition syndromes, developing early disease detection applications, and investigating preventative treatment approaches.

#### ENHANCE

Enhance precision medicine by using the most advanced preclinical model systems to investigate and define intelligent and effective treatment combinations at scale, to provide real-time data-driven patient treatment recommendations.

#### ESTABLISH

Establish the capacity for developing a series of previously undruggable paediatric cancer targets, for future development as novel, and potentially less harmful, paediatric cancer drugs.



Professor Maria Kavallaris AM

### The Benefit

Over the past 40 years, Children's Cancer Institute has worked tirelessly to improve lifelong survival for Australian children with cancer, and are now uniquely positioned to achieve the ambitious aim of preventing death from childhood cancer.

The ACCEPT Program will revolutionise childhood cancer care by advancing early detection, prevention, and treatment. It will improve understanding of child cancer predisposition and risk, enhance precision medicine through cutting-edge models, and develop targeted therapies for previously untreatable cancers, ultimately aiming to prevent childhood cancer deaths and improve patient outcomes.

## Building Blocks



The ZERO Childhood Cancer Program is a world-leading precision medicine program for children with cancer which brings together leading clinicians and researchers around Australia and internationally, embracing research-driven clinical care to achieve better outcomes for children with cancer, now and into the future.

### ACRF Child Cancer Liquid Biopsy Program



A 2019 ACRF-funded program working to reduce the painful and invasive procedures associated with cancer care through developing more sensitive but less harmful blood or lymph fluid biopsies.

### ACRF Spatial Immune-oncology Research (ASpiRe) Program



ACRF supported research looking at unlocking the potential of immunotherapies for childhood cancers.

## Use of Funds

The \$5M investment in infrastructure ecosystem will be housed in the new purpose-built and uniquely designed Minderoo Children's Comprehensive Cancer in Randwick, scheduled to open before the end of 2025. This will be the new home for Children's Cancer Institute, together with the clinical, research and allied health staff of the Kids Cancer Centre and Sydney Children's Hospital Network. The partnership also includes the University of New South Wales.

Technology	Cost
<b>Early detection and prevention:</b> Sample handling and biobanking Gene editing equipment Predisposition testing (reagents) Gene editing (reagents)	\$80,000 \$121,000 \$180,000 \$175,000
<b>Advanced treatments:</b> ALTEN Microfluidics (pumps, antivibration table, chip manufacture) Rastrum 3D bioprinter ALTEN (reagents) Bioprinting (reagents) Multiomics and single cell (reagents)	\$70,000 \$80,000 \$125,000 \$100,000 \$200,000
<b>New therapeutics:</b> Liquid handling and automation (Modular automation workstation, Echo acoustic dispenser, Agilent Bravo liquid handler, automated incubator) Imaging and assay detection (Opera Phoenix Plus and AMNIS) DrugSeq (reagents) Drug screening (reagents)	\$1,280,000 \$1,500,000 \$139,000 \$200,000
Salary support	\$600,000
Computing	\$150,000
<b>Total</b>	<b>\$5,000,000</b>

## Meet the Team

The ACCEPT will build on the expertise and track record of the investigative team, who are internationally regarded in their respective fields. The team includes both established and emerging research leaders in their associated fields, with diversity and inclusion carefully considered as part of the selection criteria.



**Chief Investigator  
Michelle Haber AM**  
Executive Director, Children's  
Cancer Institute



**Chief Investigator  
Glenn Marshall AM**  
Group Leader – Embryonal Cancer  
Therapy and Prevention, Children's  
Cancer Institute, Paediatric  
Haematologist/Oncologist, Kids  
Cancer Centre

**Chief Investigator Noemi Fuentes-Bolanos**

Post Doctoral Scientist – Germline Cancer Risk, Children's Cancer Institute  
Paediatric Oncologist and Cancer Genetics Fellow – Kids Cancer Centre

**Chief Investigator Mark Pinese**

Team Leader – Genomic Childhood Cancer Risk, Children's Cancer Institute

**Chief Investigator Maria Kavallaris AM**

Team Leader – Cancer Epigenetic Biology and Therapeutics  
Theme Head – Therapeutic Discovery, Children's Cancer Institute

**Chief Investigator David Gallego Ortega**

Head of School (Acting) – School of Biomedical Engineering  
Head – Functional Genomics Laboratory  
Director – Single-Cell Technology Facility, University of Technology Sydney

**Chief Investigator Fatima Valdes**

Team Leader – Cancer Epigenetic Biology and Therapeutics  
Theme Head – Therapeutic Discovery, Children's Cancer Institute

**Chief Investigator Emmy Dolman**

Research Leader – Translational Drug Testing and Pharmacogenomics, Zero Childhood Cancer  
ex vivo tumour drug response profiling initiative, Children's Cancer Institute

**Chief Investigator Ian Street**

D Head, THERapeutic INnovation for Kids (THINK), Children's Cancer Institute

**Chief Investigator Antoine de Weck**

Group Leader – Computational Drug Discovery Biology, Children's Cancer Institute

## 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 Childhood Cancer Early Detection, Prevention and Treatment Program has the potential to achieve:

### HUMAN

- There has been significant progress in the treatment of paediatric cancers with more than 80% of children expected to survive into adulthood. Despite this, at least 60% of survivors develop chronic health conditions and up to 80% experience severe or life-threatening complications<sup>1</sup>. The ACRF Childhood Cancer Early Detection, Prevention and Treatment Program has the potential to transform the long-term outlook for childhood cancer survivors.
- Australian children with cancer now have access to a national precision medicine program (ZERO). The samples, tools and expertise from ZERO alongside locally developed novel technologies<sup>2-4</sup> will be leveraged by The ACRF Childhood Cancer Early Detection, Prevention and Treatment Program to improve diagnostic tests, guide treatments and develop new drugs and provide a unique opportunity for all children diagnosed with cancer in Australia.

### LEVERAGE

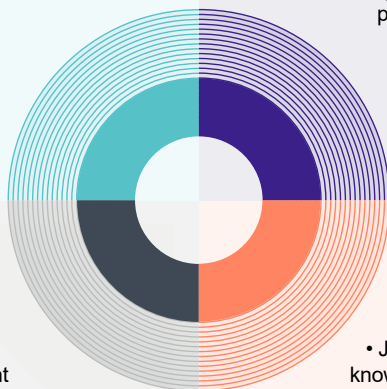
- Over the last five years the research team have secured over \$135M in competitive grant funding. The investment in The ACRF Childhood Cancer Early Detection, Prevention, and Treatment Program would significantly strengthen future grant applications and secure additional funding.
- Of the \$78Bn net present gains generated by medical research from 1990 to 2004, \$52B was in the form of health gains and \$26B in wider economic gains<sup>5</sup>. Extrapolating these figures, the \$5M invested by The ACRF Childhood Cancer Early Detection, Prevention, and Treatment Program has a potential return of \$19.5M - \$13M in the form of health gains and \$6.5M in the form of wider economic gains.
- Additional funding totalling \$2.8M will be provided by the University of New South Wales (\$2.5M) and Cancer Institute NSW (\$500,000) to support the development of The ACRF Childhood Cancer Early Detection, Prevention, and Treatment Program.

### SOCIETAL

- Adult survivors of childhood cancers are more likely to be in poorer health, need assistance with personal care and routine needs, have work limitations, be unable to work because of health, miss more days of work, and have greater household productivity. The annual productivity loss for adult survivors of childhood cancer is estimated to be \$12,000 per person compared with \$4,800 per person for individuals without a history of cancer<sup>1</sup>. The ACRF Childhood Cancer Early Detection, Prevention and Treatment Program has the potential to greatly enhance the long-term outcomes for childhood cancer survivors thereby reducing productivity losses.
- The ACRF Childhood Cancer Early Detection, Prevention and Treatment Program 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<sup>6,7</sup>. Based on the average Australian wage, and taking into consideration the labour force participation and unemployment rate, this accounts for an annual productivity loss of \$14,467 per caregiver annually.

### 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 \$375,200 in value added gain<sup>5</sup>.
- One of the most important outputs of The ACRF Childhood Cancer Early Detection, Prevention, and Treatment Program will be publications to inform future research. The \$5M invested by ACRF alone has a potential return of 58 publications<sup>5</sup>.



For references, please visit [acrf.com.au/philanthropy-accelerate-references](http://acrf.com.au/philanthropy-accelerate-references)

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To find out more about ACRF Accelerate and this exciting project please contact [philanthropy@acrf.com.au](mailto:philanthropy@acrf.com.au) 1300 884 988

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