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Foreword

At Children's Cancer Institute, our mission is to transform discoveries into real-world solutions that improve lives. Guided by our vision to save the lives of all children with cancer and improve their long-term health, we remain committed to advancing and applying medical research to cure or prevent cancer in children and adolescents.

The 2025 Research Impact Report highlights a year of meaningful progress across research, translation, and collaboration at Children's Cancer Institute. Our teams continued to advance new technologies, strengthen partnerships, and deliver research with real-world benefit for children with cancer and their families.

Our values,

- Challenge today, change the future
- Achieve as one
- Balance head and heart
- Own it, do it

remain central to how we work. They guide our efforts to generate new knowledge, build research capacity, improve health outcomes, and enhance the social and economic impact of our science.

Throughout 2025, we focused on strengthening engagement with the Research Impact Framework and supporting researchers to document the breadth of their contributions. This report reflects that collective effort and showcases the progress made across the Institute as we continue working towards better outcomes for children with cancer.



Spotlight on **2025**

166
Staff & Students entered impact



2009
Impacts entered in 2025



90%
Engagement by Staff & Students **



6991
TOTAL IMPACTS ENTERED

ORGANISATIONAL ENGAGEMENT

2025 marked the second year of the CCI Impact Repository being fully implemented. All research staff and postgraduate students were encouraged to record their impact contributions for the year, as well as any retrospective impacts from previous years. Since the repository's launch in 2024, 6,991 impact records from 178 staff and students have been captured. In 2025 alone, 166 contributors added 2,009 new records, a substantial increase from the 1,186 impacts entered in 2024 by 122 contributors, demonstrating strong and growing engagement with the Impact Framework.

This includes notable improvements across several staff cohorts, reflecting targeted efforts throughout the year to build awareness and emphasise the value of identifying and recording impact.

Research Leaders: 100% (up from 92% in 2024)

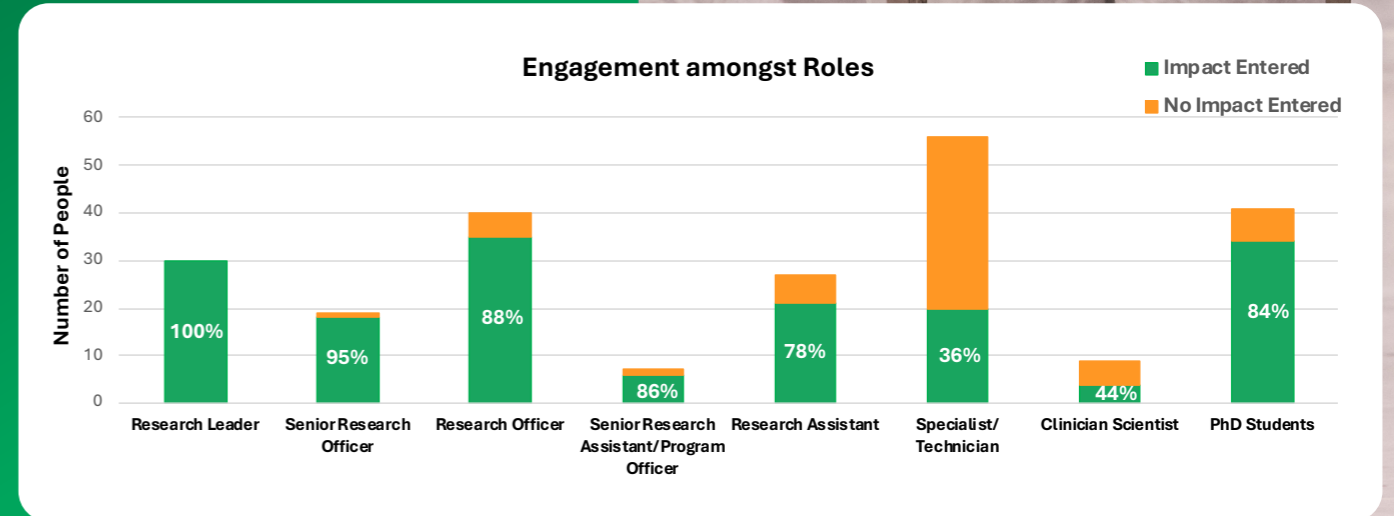
Research Assistants: 78% (up from 53% in 2024)

PhD students: 84% (up from 65% in 2024)

Specialists/Technicians: 36% (up from 16% in 2024)

While engagement from technicians and specialists remained lower relative to other groups, likely due to the service-oriented or technical nature of their roles (e.g. software engineering, product design, platform support), there was still a notable improvement compared to 2024.

The overall compliance rate increased to 90%**), up from 78% in 2024, underscoring strong organisational uptake of the Research Impact Framework in its second year.

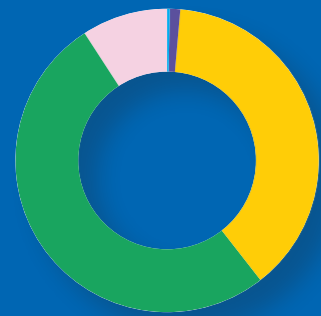


*Honours students, interns and visiting students, due to the short-term nature of their role

**Specialists/technicians that did not enter any impacts/contributions

Children's Cancer Institute

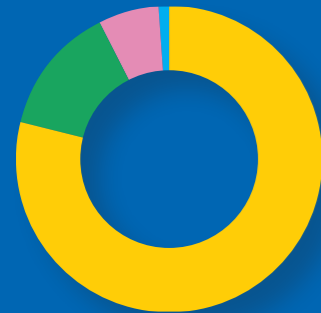
Impact Summary



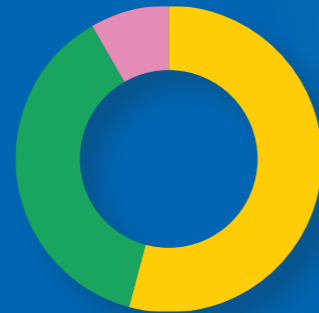
Research Officers



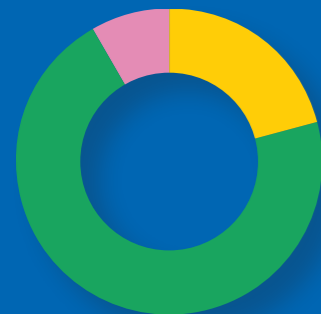
Clinician Scientists



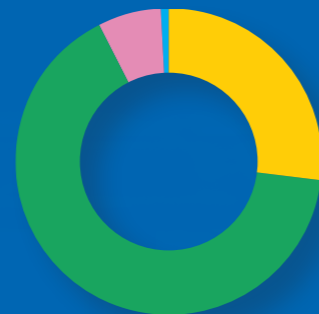
PhD Students



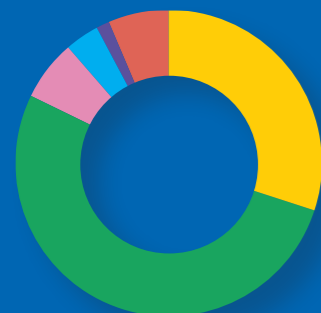
Specialists/Technicians



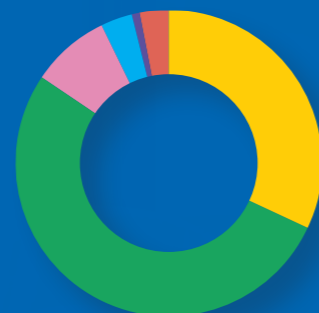
Senior Research Assistant/Program Officer



Research Assistant



Research Leaders



Senior Research Officers

Key

- Knowledge Impact
- Research Capacity Building
- Health
- Social
- Economic
- Informing Decision Making

2009

IMPACTS ENTERED FOR 2025

2025 Highlights



KNOWLEDGE IMPACT

- 89** Peer-reviewed Publications
- 49%** with our researchers as first/senior author
- 85%** publications in Q1-ranked journals

- >4,790** citations received in 2025

- 119** Invitations to Peer Review

- 280** Presentations Delivered incl.
- 85** Invitations to present

- 33** Presentation Awards

- 49** Awards/Recognitions



RESEARCH CAPACITY BUILDING

- 188** Research Staff

- 72** Students incl

- 41** PhD Students

- 47** Researchers who have actively trained/ mentored colleagues

- 13** New Conjoint appointments
- 10** Academic Progressions
- 14** Internal Researcher Promotions

- 150** Research Agreements signed with organisations worldwide

- 14** Active discussions with Global Industry Partners

- 40** Researchers have participated in a Conference Organising/Program Committees



INFORMING DECISION MAKING

- >44** national and international strategic panels or committees with active researcher involvement

- >21** external advisory boards supported through expert advice from researchers

- 160** engagements with government stakeholders

- ~20** government policy consultations supported through expert input



ECONOMIC/SOCIAL/ HEALTH IMPACT

- >26** Clinical Trials supported by CCI researchers/clinician scientists

- 48** New Research Staff (Jobs Created)

- 60** New Grants totalling \$60,681,438

- 4** Active Contract Research Agreements

- 110** visitors toured the Institute led by 25 Researchers

- >90** Occasions of Public Engagement through seminars, fundraising events, and community outreach



Our teams continued to advance new technologies, strengthen partnerships, and deliver research with real-world benefit for children with cancer and their families.

Advancing knowledge

89
Peer-Reviewed Publications

49%
with our researchers as first/senior author

>50%
of papers with international collaboration*

85%
in the top 25% of journals (Q1-ranked)*

37%
in the top 5% of journals**

30%
with Impact Factor >10

In 2025, our publications were cited
>4700 times**

INCLUDING
> 125
citations for papers published in 2025*

* As reported by SciVal
** As reported by Scopus



Cancer Biology Theme Research Highlights from 2025

NEW GENETIC VARIANT IN CHILDHOOD CANCER REVEALS OPPORTUNITY FOR TARGETED THERAPY

Researchers at Children's Cancer Institute have discovered a previously unknown genetic alteration in childhood cancer that could unlock new treatment options using existing drugs. Published in *NPJ Precision Oncology*, the study highlights how advanced genomic analysis is driving breakthroughs in personalised cancer care.



Dr Lauren Brown



Prof Paul Ekert

Childhood Cancer Program (ZERO), which matches treatments to each child's unique tumour profile

- **Tumour-agnostic approach:** Instead of treating based on cancer type, researchers aim to match therapies to genetic variants, potentially benefiting both paediatric and adult patients
- **Broader impact:** Identifying "missed therapeutic opportunities" accelerates access to effective treatments without waiting for new drug development

Why it matters

This finding demonstrates the power of precision medicine to uncover hidden treatment options, offering hope for children with hard-to-treat cancers and paving the way for more personalised, effective care.

Greater understanding of cancer risk in children

Research from the Genomic Childhood Cancer Risk team have uncovered that 39% of children with cancer have no known reportable genetic risk. Their research has demonstrated that conducting genetic screening in children with cancer has clinical value and that genomics combined with functional modelling shows great promise in preventing childhood cancer.

Key Highlights

- **New genetic target identified:** A novel variant in the NTRK2 gene, an internal tandem duplication, was found in a child with a rare brain tumour (CNS neuroblastoma). This is the first time this type of alteration has been reported in NTRK2
- **Therapeutic opportunity:** Laboratory modelling showed the variant is highly sensitive to tyrosine kinase (TRK) inhibitors, a class of drugs already approved for other cancers. This means these drugs could be repurposed for children with this variant
- **Precision medicine in action:** The discovery was made through whole genome sequencing in Australia's Zero



ADVANCING TARGETED THERAPIES FOR PAEDIATRIC LEUKAEMIA: Antibody-Drug Conjugates Show Promise

A new study highlights the potential of antibody-drug conjugates (ADCs) to improve treatment for children with relapsed or refractory acute lymphoblastic leukaemia (ALL). Researchers evaluated pivekimab sunirine (PVEK), an ADC that targets CD123, a protein highly expressed in ALL cells, and delivers a potent cytotoxic payload.

Key Highlights

- **Promising efficacy:** In preclinical testing across 39 paediatric ALL patient-derived xenograft (PDX) models, PVEK significantly extended survival, with a median event-free survival of 57 days after three weekly doses

Subtype advantage

- B-lineage ALL showed higher CD123 expression and better response to PVEK compared to T-lineage ALL
- PVEK treatment cleared leukaemia cells from hemato-lymphoid organs in B-ALL models

Mechanistic Insights

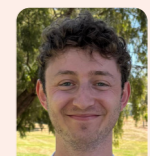
- CD123 expression alone did not predict response, suggesting other factors influence drug activity
- Resistance was linked to failure of antibody internalization, despite sensitivity to the payload, revealing a novel resistance mechanism

Clinical Relevance

Findings strongly support clinical translation of PVEK for B-lineage paediatric ALL, offering a new targeted option for children with hard-to-treat disease.

Why it matters

This research demonstrates the potential of ADCs to deliver highly effective, precision-based therapies for paediatric leukaemia, addressing urgent needs for children who relapse after standard treatment.



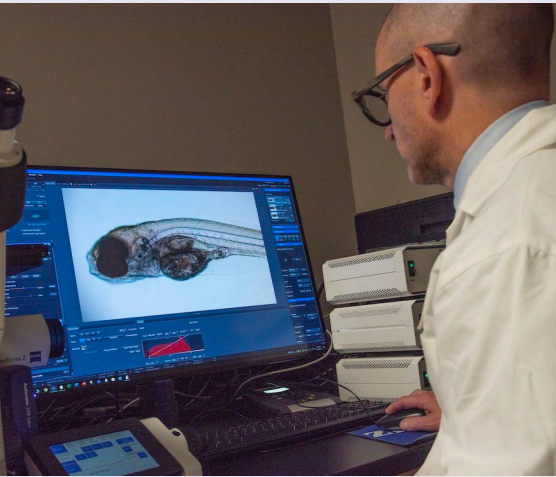
Mr Ben Watts



Dr Christopher Smith



Prof Richard Lock



Therapeutic Discovery Theme

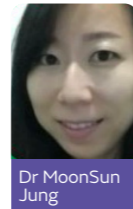
Research Highlights from 2025

A POWERFUL NEW TOOL FOR PRECISION ONCOLOGY

CCI researchers, led by **Professor Maria Kavallaris AM**, have pioneered a rapid and advanced method for growing 3D tumour models ("tumouroids") using living cancer



cells from children. This breakthrough enables high-throughput drug testing to identify the most effective treatment for each child in just days, compared to months with traditional methods. To develop the model, researchers used advanced 3D bioprinting technology



Dr MoonSun Jung

and a specially engineered matrix (hydrogel system) that mimics a tumour's natural environment. Using cancer cells from children with two of the more commonly diagnosed childhood tumours, neuroblastoma and sarcoma, they then created patient-specific 'tumouroids'.

Published in *EMBO Molecular Systems Biology*, the innovation is set to transform precision medicine globally. The technology addresses key challenges such as limited tumour samples and lengthy model development times, ensuring tumouroids accurately replicate patient tumours for reliable drug sensitivity testing. This approach promises:

- **Faster, personalised cancer care** for children
- **Improved clinical outcomes** through timely treatment matching
- **Acceleration of new therapy development** for hard-to-grow cancers



Dr Valentina Poltavets



Prof Maria Kavallaris

A novel technique for preclinical testing of brain tumour treatments

Researchers from the Brain Tumour Group have established a precise stereotaxic method for creating orthotopic patient-derived xenograft (PDX) models of paediatric brain tumors, enabling clinically relevant preclinical testing by accurately replicating tumor biology and brain microenvironment for improved therapeutic development.

A novel therapy for DMG

High-throughput screening and *in vivo* studies identified fenretinide as a brain-penetrant therapy that significantly improves survival in diffuse midline glioma, offering a breakthrough for one of the deadliest paediatric brain cancers, diffuse midline glioma.

Two New Treatment Strategies for high-risk neuroblastoma

Researchers from the Experimental Therapeutics and Molecular Oncology team have identified:

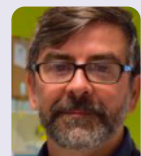
1

Lowering arginine levels with the novel agent BCT-100 extends survival of mice with high-risk neuroblastoma, and also improves their response to standard chemotherapy and immunotherapy, with no increased toxicity.

2

An iron-chelating small-molecule MYCN inhibitor M606 selectively targets neuroblastoma cells with high MYCN levels, and delays tumor growth in mice.

BRIDGING RESEARCH AND CARE: ZEBRAFISH MODELS TRANSFORM TREATMENT DECISIONS



A/Prof Jamie Fletcher



Prof Michelle Haber

A first-of-its-kind proof-of-principle collaborative study between CCI and CHEO Research Institute/University of Ottawa (Canada) demonstrates that **larval zebrafish models** are an effective tool to help guide clinical decision-making in real time for challenging paediatric cancer cases, especially when molecular profiling fails to identify actionable targets. Published in *Cancer Research Communications*, this study compared zebrafish patient-derived xenograft (PDX) models with mouse PDX models and actual clinical outcomes, showing zebrafish accurately predicted responses to 11 of 12 treatment regimens.

- **Addresses a critical gap:** 30% of high-risk paediatric cancers lack actionable molecular targets, limiting treatment options
- **Faster, cost-effective modelling:** Zebrafish PDXs require smaller tumour samples and deliver drug response data more quickly than mouse models
- **Clinical relevance:** For three cases where mouse models failed, zebrafish provided actionable insights that mirrored real patient outcomes
- **Future potential:** Enables prospective modelling to guide treatment decisions in real time, improving survival and quality of life for children with cancer

This innovation represents a major advance in precision medicine, bridging the gap between research and clinical care for the most challenging paediatric cancer cases.

Clinical Translation Theme

Research Highlights from 2025

GENETIC INSIGHTS INTO DIFFUSE MIDLINE GLIOMAS REVEAL NEW AVENUES FOR TARGETED THERAPY

An international study led by Children's Cancer Institute and Kids Cancer Centre, Sydney Children's Hospital, has provided critical insights into diffuse midline gliomas (DMGs), an aggressive childhood brain cancers that is almost always fatal within a year of diagnosis. Published in *Neuro-Oncology*, this is the largest study of its kind, analyzing 252 patients, including 153 with DIPG.

Key Findings

Genetic predisposition uncovered:

- 7.5% of children carried pathogenic germline variants in cancer predisposition genes such as BRCA, previously linked to breast and ovarian cancer
- Among those with family history data, 25% had relatives with early-onset breast/ovarian cancer

Clinical implications:

- Oncologists should consider germline testing for children with DMGs, especially if there is a family cancer history

- Findings may influence treatment strategies and inform genetic counseling for families

Therapeutic breakthrough:

- One child with relapsed DMG and BRCA2/FANCE variants had a near complete response to a novel drug combination: olaparib (PARP inhibitor) and durvalumab (immune checkpoint inhibitor)

Future directions:

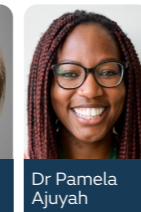
- Research will focus on understanding gene alterations driving DMGs and developing targeted therapies

Why it matters

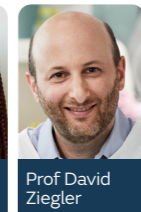
This study not only reveals how inherited genetic changes may contribute to deadly brain cancers but also points to new treatment opportunities, offering hope for families facing these devastating diagnoses.



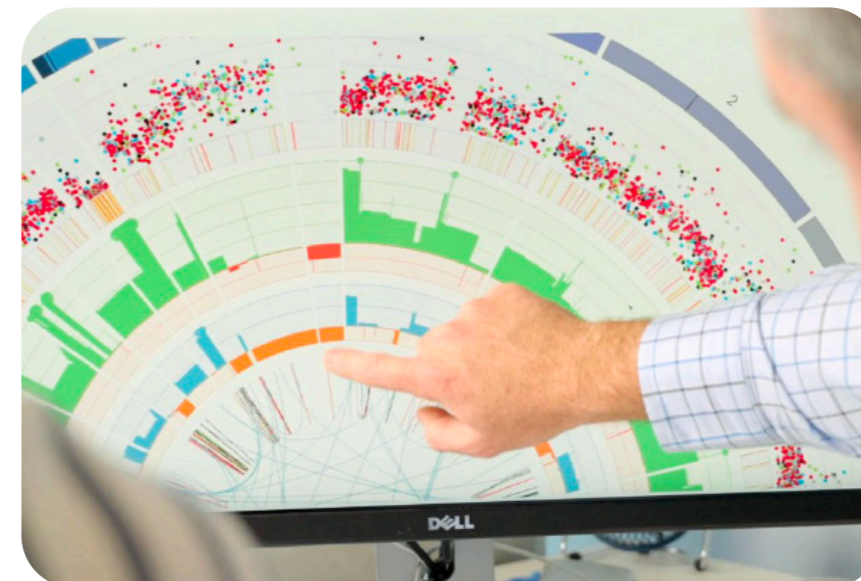
Dr Marion Mateos



Dr Pamela Ajuyah



Prof David Ziegler



Prof Mark Cowley



Dr Patricia Sullivan

IMPROVING GENOMIC INTERPRETATION FOR RARE DISEASES AND CANCER

The Challenge

Families facing childhood cancer or rare genetic disorders often expect a quick, accurate diagnosis, the first step toward effective treatment. Yet, for many, this isn't reality. A major barrier is the complexity of the human genome: thousands of genetic changes can appear in a single patient, and many remain poorly

understood. Among the most elusive are splice-altering variants, which disrupt gene splicing and account for up to one-third of disease-causing mutations. Until recently, these variants were difficult to detect and interpret, leaving clinicians without clear answers.

The Approach

Researchers in the Computational Biology group developed a suite of innovative tools to close this diagnostic gap:

Firstly, in 2023 they published:

- **Introme** – A machine learning algorithm that identifies subtle splicing disruptions missed by conventional tools

Then in 2025, they published:

- **SpliceVarDB** – The largest curated database of experimentally validated splice-altering variants (>50,000 entries across 8,000 genes), enabling rapid classification without extensive lab work
- **Predictive Splicing Rules and Models** – Data-driven frameworks that provide clinicians with clear guidance for assessing splicing potential

These resources are freely accessible, supporting precision medicine programs worldwide, allowing bioinformaticians to integrate these predictive tools into genomic workflows. They are already transforming precision medicine by accelerating and enabling clinicians and diagnostic laboratories to interpret and classify variants faster and more accurately, reducing uncertainty and improving treatment decisions. Patients and families benefit from faster, more accurate diagnoses and tailored care.

Why It Matters

Precision medicine is revolutionising care by matching treatments to the unique genetic profile of each patient. Programs like Zero Childhood Cancer already show that genomic analysis can identify disease-causing variants in over 90% of children with cancer. The impact of these tools is significant: increased diagnostic yield for rare diseases and childhood cancers, reduced duplication of costly lab validation, and strengthened capacity for personalised medicine, bringing us closer to ensuring every child receives the right diagnosis and the right treatment at the right time.

Knowledge Dissemination

280
Presentations delivered by our researchers at conferences/seminar series

103
Poster Presentation

177
Oral Presentations

75
of these were at International Conferences

86
of these were Invited Presentations

12
were Keynote/Plenary Presentations

16
Invitations to Participate in Panel Discussions/Roundtables



Examples include:

- **Rare Cancer Australia**
Maximising Rare Cancer Clinical Trials;
- **World Cancer Leaders Summit**
AI in Cancer Care: From Genomics to Prevention Support;
- **European Forum of Good Clinical Practice**
Innovative Approaches for Clinical Trials in Small Population



Above: Dr Zan Dai presenting at the International Nanomedicine Conference in Sydney



Lakshika Keerthirathna (PhD student), Prof. Maria Kavallaris and Dr Amy Logan at the Controlled Release Society Annual Conference held in Philadelphia, USA



Above: Dr Holly Holliday, A/Prof. Fa Valdes Mora and Dr Hansen Kosasih at the Gordon Research Conference: Cancer Genetics and Epigenetics (Lucca, Italy)



Prof. Paul Ekert presenting at the Collaborative Centre for Genomic Cancer Medicine Lecture series at Peter MacCallum Cancer Centre



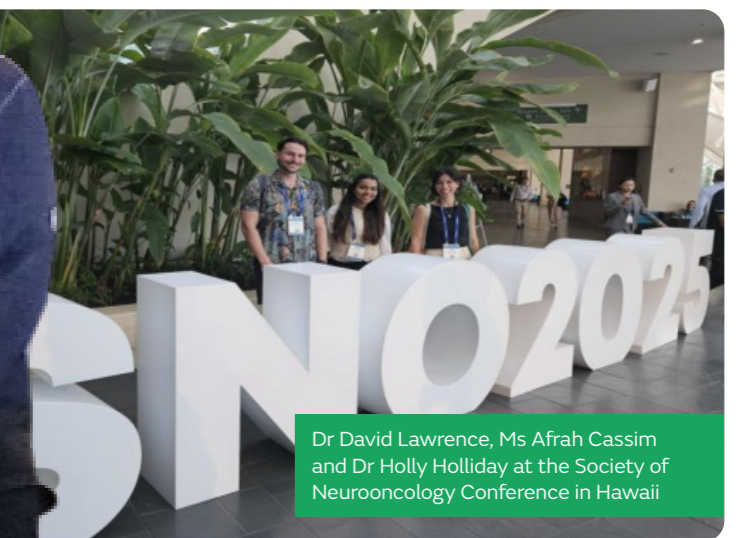
Above: The Functional Genomics of Leukaemia team at the European Haematology Association conference in Milan, Italy.



Prof. Mark Cowley at the AACR Paediatrics meeting, Boston



CCI representation at the AACR Paediatrics meeting, Boston. From Left to Right, Prof. Louis Chesler, Paulette Barahona, Patricia Sullivan, Erin Coll, Dr Noemi Fuentes Bolanos, Chelsea Mayoh, Prof. Mark Cowley and Prof. Paul Ekert. Six posters and three oral presentations were delivered.



Dr David Lawrence, Ms Afrah Cassim and Dr Holly Holliday at the Society of Neurooncology Conference in Hawaii

Recognising Research Excellence

In 2025, many of our researchers were recognised by leading national and international organisations for their outstanding contributions to science and innovation. These prestigious awards span every career stage, from PhD students and early-career researchers to mid-career scientists and senior leaders, and reflect the widespread impact of their work, advancing knowledge, shaping clinical practice, and driving progress in childhood cancer research. From competitive fellowships to national and international accolades, these recognitions underscore the calibre of research conducted at our Institute and its influence on the broader scientific community.



Awards and Recognition

82

Awards/Honours received by our researchers

28

Travel Grants

6

Scholarships/Fellowships

33

Prizes awarded at conferences/symposiums

19

Oral Presentations Prizes

14

Poster Presentations Prizes



Ms Chelsea Mayoh 2025 CINSW Rising Star PhD Candidate Award



Ms Lakshika Keerthirathna, (far left) **Dr Lauren Brown**, (second from left), **Ms Lara Knight** (far right), and **Dr Megan Rumford** (not pictured) all won oral presentation prizes at the Kids Cancer Alliance Symposium



Prof. Richard Lock elected as the Donald Metcalf orator for NDLR 2026



Dr Aaminah Khan 2025 AAMRI Rising Star Award Finalist



Prof. Maria Kavallaris Fellow of the American Institute for Medical and Biological Engineering (AIMBE) and Fellow of the Controlled Release Society



Prof. David Ziegler Elected Fellow of the Australian Academy of Health and Medical Sciences



Dr Ernest Moles Moderna Australia Research Fellowship



A/Prof. Emmy Fleuren Col Reynolds Fellowship The Kids Cancer Project



Prof. Michelle Haber Royal Society NSW, James Cook Medal for 2025 & LEMBERG Medal for 2025- Australian Society for Biochemistry and Molecular Biology



Dr Dona Johns Shortlisted for Falling Walls Lab-Young Innovators

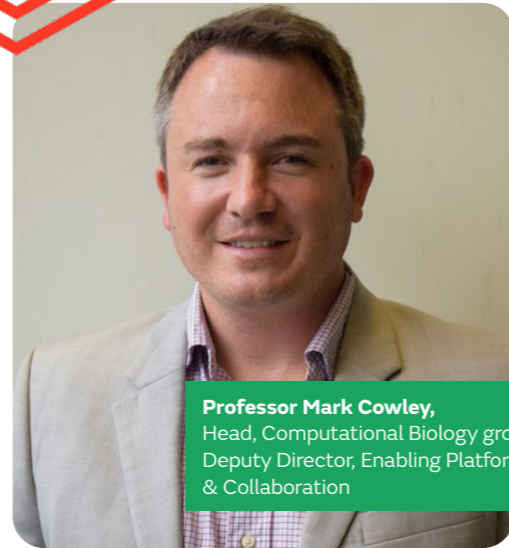


A/Prof. Loretta Lau AMGEN-ACRF Women in Science Preceptorship UNSW Discipline of Paediatrics and Child Health Publication Prize (Senior Academics Category).

CCI wins the Databricks ANZ Data + AI for Good Award



In December 2025, Children's Cancer Institute (CCI) was recognised by Databricks ANZ for the innovative use of data and AI to accelerate life-saving research. By implementing a Lakehouse architecture on the Microsoft Azure Databricks platform, CCI has unified genomic, clinical, and treatment data at scale, unlocking insights that were previously trapped in siloed systems. This innovation enables researchers to analyse billions of genomic variants in minutes, not days, and apply advanced machine learning to personalise therapies for children with rare and high-risk cancers.



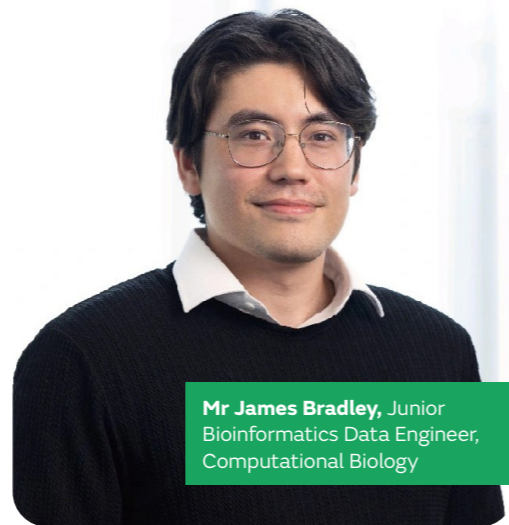
Professor Mark Cowley,
Head, Computational Biology group
Deputy Director, Enabling Platforms & Collaboration

The impact:

Faster translation of genomic data into clinical insights

New models of precision medicine for paediatric oncology

Global data sharing to advance research collaboration

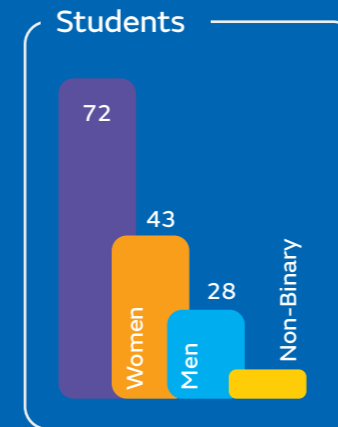
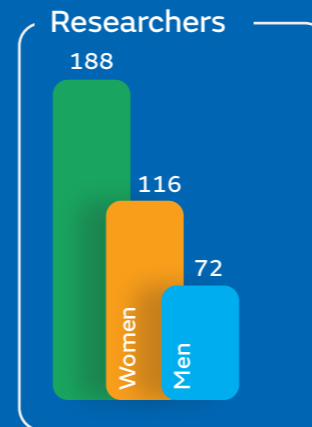


Mr James Bradley, Junior
Bioinformatics Data Engineer,
Computational Biology

Every dataset represents a child, a family, and a chance to change the outcome. By harnessing the power of data and AI, CCI is not just advancing science, it is changing lives.

Research Capacity building

Our Researchers and Students in 2025



188
Research Staff
38% Men, 62% Women

72
Students
40% Men, 60% Women

48
New Starters in 2025

11
Researchers with an h-index of > 40*

22
Researchers with an FWCI > 2**

*An h-index of 40 is proposed to characterise outstanding scientists likely to be found only at the top universities or major research labs (Hirsch 2005 PNAS). Source: SciVal.

** Greater than double the world average FWCI of 1.0



Researcher Roles

- Research Leader
- Senior Research Officer
- Research Officer
- Senior Research Assistant/Program Officer
- Research Assistant
- Specialist/Technician
- Clinician Scientists



Students

- PhD
- PhD-New students
- Honours
- Interns/Visiting Students



Career Development

2025 brought a renewed focus on career development for CCI researchers, with several new initiatives developed to help researchers progress their careers.

A simplified promotions application process and pathways to progress to independence at a mid-career level

A new internal promotion pathway was created for Senior Scientists to advance to Team Leader positions, ensuring that established research talent has access to predictable leadership progression opportunities.

The Senior Scientist position description was clearly distinguished into 2 different tracks (one for academic leadership and the other for technical leadership).

Internal Researcher Promotions

14 Researchers were promoted internally

2 successful Senior Scientist (Academic) roles



The CareerYOU program is an evidence-based professional development workshop designed to support women in STEM to reflect on their career trajectory and build tools for future growth. Across two days, the program guided participants through identifying and leveraging their strengths, seeking constructive feedback from colleagues and mentors, refining future career goals, and mapping the tangible steps needed to progress. The workshop also explored values-based career planning, adopting a growth mindset, and developing a strong professional network. Participants heard from an inspiring panel of women in research and worked through practical strategies for mentoring, sponsorship, and setting developmental priorities for the next 12–18 months. A unique aspect of the program was the formation of “accountability buddy” groups, enabling continued peer support beyond the workshop.



Overall, I found the CareerYOU program incredibly insightful and empowering. It gave me the space to reflect on where I am in my career and where I want to go, and most importantly helped me map out clear, actionable steps to get there. Having accountability buddies from outside the Institute has added an extra layer of motivation and support. The program has genuinely strengthened my confidence and equipped me with practical tools that will guide my career progression over the coming years “

Dr Alice Salib, Research Officer

Participating in a cross MRI mentoring program

10 Researchers (5 mentors and 5 mentees) from CCI participated in a cross MRI mentoring program this year.

Co-ordinated by the Garvan Institute of Medical Research, this program enabled our people to connect with, network with, and learn from others across the MRI landscape.

Investing in targeted programs to support women in research

Through our partnership with Franklin Women, we were able to offer four women unique developmental experiences.

2 women were mentees in the Inclusive Leadership Mentoring Program, which connects mid-career women with senior leaders to foster diverse, cross-sector mentorship, driving meaningful career progression.

2 women participated in Franklin Women's CareerYOU program, for early to mid career women designed to address a critical gap in career development, empowering women in health and medical research to clarify their ambitions, set bold goals and build sustainable, values-aligned careers.

CONJOINT APPOINTMENT HOLDERS

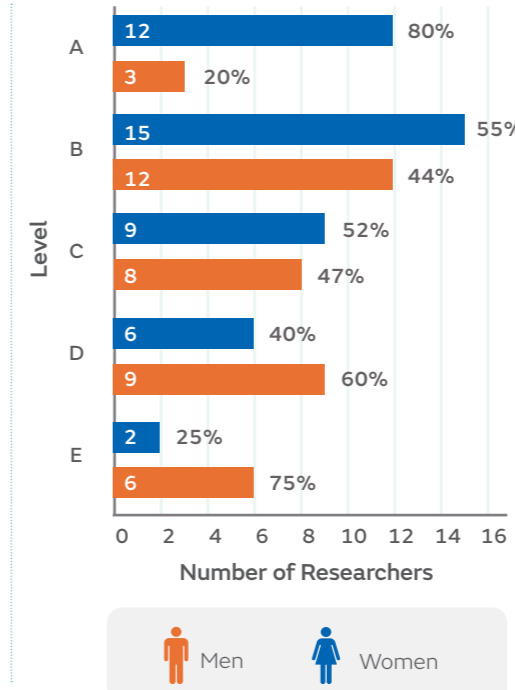
13 Researchers conferred a conjoint appointment

2 at Level A (Associate Lecturer)

8 at Level B (Lecturer)

2 at Level C (Senior Lecturer)

1 at Level E (Professor)



Building Commercialisation Capability: The Bridge Program

The Bridge Program, delivered by QUT with leading pharmaceutical companies, universities, and industry partners, is Australia's premier initiative for developing skills and networks to bring new medicines to market. Each year, 100 participants nationally are selected for intensive training in pharmaceutical commercialisation, combining online modules, seminars, and direct engagement with global pharma and venture capital networks.

3 Researchers from CCI were chosen among the 100 participants nationwide to participate in The Bridge Program.

Participation strengthens CCI's capability in drug development, accelerates pathways to clinical application, and embeds our researchers in one of Australia's most influential pharma and biotech networks.



Taking part in QUT's Bridge Program really opened my eyes to how drug development and commercialisation work beyond the lab. I loved getting to work with such a passionate group, learn from industry mentors, and stretch myself with our nanomedicine pitch – it was a steep learning curve, but definitely worth it”

Dr Varshini Venkata

ACADEMIC PROGRESSION

10 successful Academic Progressions

Level B (Lecturer)



Dr Wenhan Chen

Dr Aaminah Khan

Level C (Senior Lecturer)



Dr Jackie Huang

Dr Kenny Ip

Dr Klaartje Somers

Level D (Associate Professor)



A/Prof Mark Pinese

A/Prof Maria Tsoli

Level E (Professor)



Prof Mark Cowley

Prof Paul Ekert

Prof Kristine Barlow-Stewart

CONGRATULATIONS!

The BRIDGE Program 2025 was truly eye-opening. It brought together industry leaders, clinicians, investors, and scientists, and showed me how a bench discovery can be shaped, pitched, and translated all the way to the bedside. It gave me a whole new appreciation for the business perspectives that drive real-world impact.”

Dr Shi Yan Lee

CCI Student Success

CCI Student Association Highlights

- Student retreat held with record turnout!!
- Shut up and write sessions held!
- Successful student executive led initiatives including student coffee mornings, Pilates, Messina, outdoor bowling and BBQs. All in one year!!
- Congratulations to all Honours students of 2025 and final year PhD Students!!

72
Total Students in 2025 & 50 Supervisors

14
Interns/Visiting Students

17
Honours Students

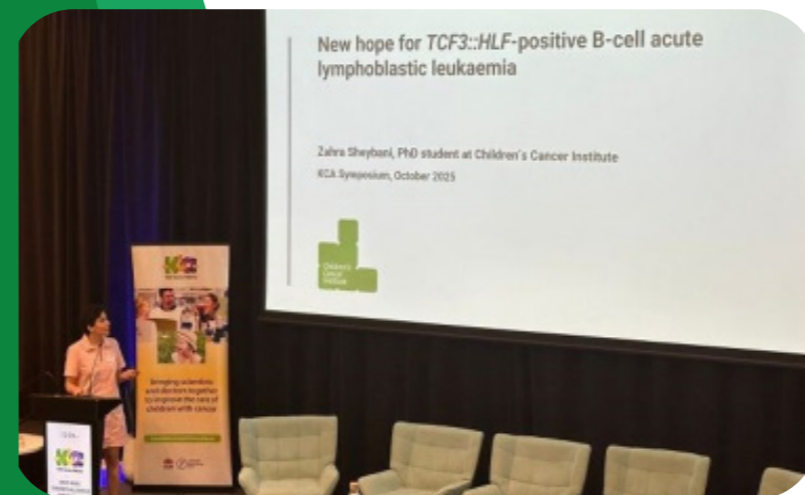
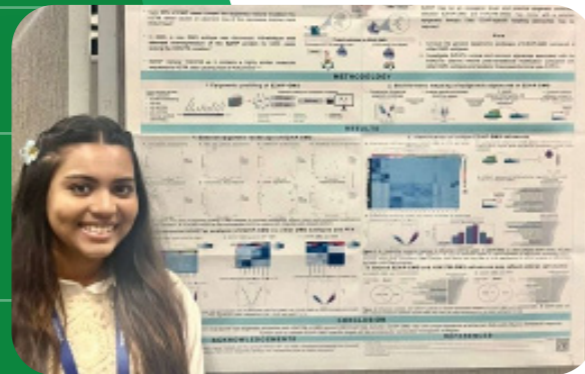
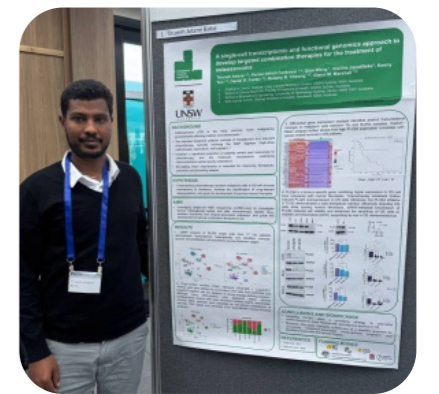
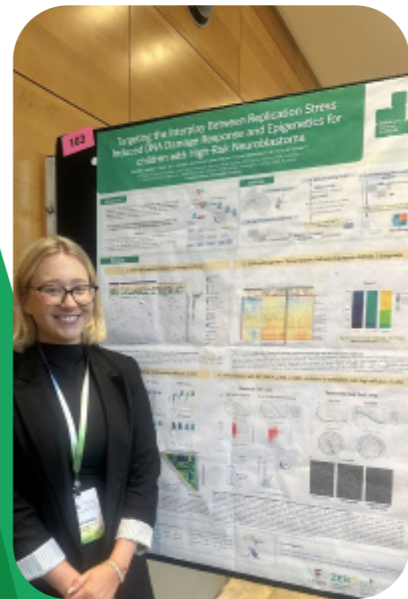
41 PhD Students → **11** New Starters in 2025

4
PhD student graduations

31
Awards received by students



52 PRESENTATIONS
delivered by PhD students, incl.
15 at international conferences



Contributions to the Field

PEER REVIEW



26
Invitations to Review Abstracts for Conferences/Symposiums

19
Editorial Board Memberships

13
Honours/PhD Theses reviewed

Right: Ms Chelsea Mayoh served as Convenor of the Cancer Bioinformatics Australia Symposium in June 2025, with Prof. Mark Cowley, Dr Piyush Mundra, Dr Christopher Smith, Dr Ben Curran, Dr Jie Mao, and Mr Sam El-Kamand on the organising committee. Their leadership in shaping the program and driving discussions reflects Children's Cancer Institute's pivotal role in advancing cancer bioinformatics nationally.

CONFERENCE ORGANISATION



9
Researchers have Chaired/ Convened a Conference or Symposium

18
Researchers have Chaired a Scientific/ Plenary Session at a Conference

47
Researchers have participated in a Conference Organising/Program Committee



CONTRIBUTIONS TO THE INSTITUTE



43
Researchers have a leadership role at the Institute
e.g., Extended Leadership Team, Enabling Platforms Lead/Chair, Animal Facilities Leadership Group, etc.)

61
Researchers participated in a Committee
e.g., Theme Council Member, Research Operations Committee, WHS Committee, etc.)

LEADERSHIP OF EXTERNAL ORGANISATIONS



25
Researchers held leadership positions in external committees/panels
eg., Chair, ANZ Paediatric Pathology Group; Deputy Chair, Cancer Genetics Special Interest Group of the Human Genetics Society of Australasia; Secretary, Australian Epigenetic Alliance; Co-Chair, Viertel Fellowship Committee, etc.)



Above: Dr Zan Dai (left) was a member of the organising committee of the 2025 Australian Society for Medical Research NSW Annual Scientific Meeting held in August 2025.

Collaborations and Partnerships

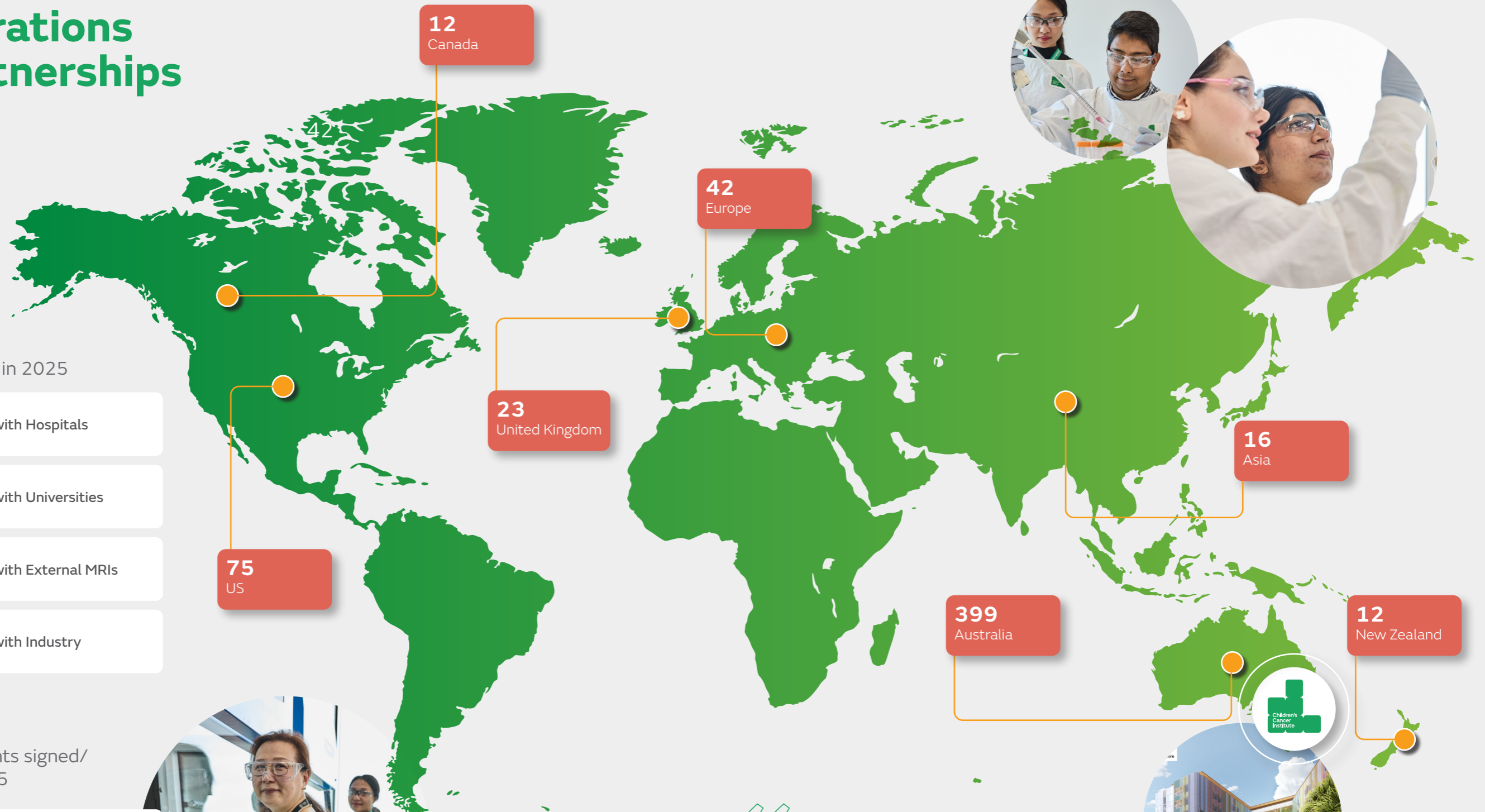


>550
Active Agreements in 2025

- >100** Agreements with Hospitals
- >100** Agreements with Universities
- >75** Agreements with External MRIs
- >50** Agreements with Industry

>150
Research Agreements signed/
commenced in 2025

- 23** Collaborative research agreements/
Multi-Institutional agreements
- 23** Material Transfer Agreements



At Children's Cancer Institute, our mission is to transform discoveries into real-world solutions that improve lives.

Enabling Platforms

Children's Cancer Institute established five Enabling Platforms in 2024 to optimise access to technology, resources, and expertise for researchers. In their second full year of operation, these platforms have demonstrated significant impact across discovery science, preclinical screening, technology innovation, and data integration. This report summarises key achievements and research impact delivered by each platform in 2025



Bioresources and Data Enabling Platform

A gateway to Institute-wide research assets, including bioresources such as patient samples, highly characterised laboratory models, and antibody/vector databases and data.

Data Chair: Dr Marie Wong Erasmus
Bioresources Co-Chairs: Dr Andrew Gifford & Angela Xie
Lead: Ms Roie O'Brien

PROGRESS TO DATE

Education Program

Mouse Models Workshop delivered with focus on good laboratory practice and mouse model applications, featuring three external speakers (UNSW, Victor Chang CRI, Sydney University) and first-time commercial sponsorship.

296 Total Attendees	23 speakers	40 presentations
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Enhanced Bioresource Visibility

Launched IdTracker portal for centralised identifier management, improved Paediatric Preclinical Biobank workflow.

4 New Databases accessible through the Hub

CCI Antibody Database

CCI Vector Library

Mouse Tolerability Database containing data for >40 drugs/combinations

PDX insights – still under construction

Capacity Building

Developed **8** unique tumour-type tissue microarrays for research applications

Completed RNAseq characterisation for **10** ZERO patient/PDX-derived culture samples

Knowledge Dissemination

Presented at Australian Biospecimen Network Association (ABNA) October 2025 and Cancer Bioinformatics Australia June 2025; manuscript in preparation on establishing mouse models educational workshop.

Bioinformatics & Research Computing Enabling Platform

Enabling impactful research through scalable, sustainable and well-supported bioinformatics and computing capabilities.

Chair: Ms Chelsea Mayoh
Lead: Mr Joe Coptly (appointed 2025)

PROGRESS TO DATE

Education Excellence

10 Bio-EDU seminars recorded (total 46 available) – including international and external speakers

22 Hacky Hours – face 2 face support

31 Datacamp users (online learning platform)

22 UNSW Students supervised across software engineering and bioinformatics projects

Infrastructure Enhancement

3 NCMAS grant applications submitted (~\$328K for 11MSU + 178TB storage)

Optimised data management by deleting **130TB** duplicated data (annual savings \$23.4K)

Negotiated new agreement with lower prices – potentially save \$40K pa based on 2025 usage

Pipeline Development

Released new analysis pipelines (nf-Sarek, nf-carbonite, nf-cutandrun, HiC) and achieved 236% efficiency increase for nf-Oncoanalyser (per-sample cost reduction from \$210 to \$60).

Support Infrastructure

Demonstrated critical demand for computational support:

494 Bioinformatics requests addressed

Implemented JIRA Service Desk for all Enabling Platforms

47 tickets processed

National Leadership

Convened Cancer Bioinformatics Australia (CBA) Conference; participated in organising committee for Australasian Genomics Technologies Association (AGTA); presented at Australian Bioinformatics and Computational Biology Society (ABACBS) as National Speaker.

Functional High Throughput Technologies

Platform Lead: Dr Tim Failes

Enabling automated robotic systems and high throughput platforms for the acquisition and analysis of complex, information-rich functional data.

PROGRESS TO DATE

Enhanced Imaging Infrastructure

Deployment of Opera Phenix Plus high-content screening system transformed screening workflows, enabling high-throughput assays and multiomics data integration.

National Leadership

Led Functional High Throughput Technologies Australia (FHTTA) partnership network, Australian Lead Identification Discovery Consortium (ALIDC) as Consortium Lead, and chaired sessions at Organoid Nexus 2025, positioning CCI as a key node in Australia's high throughput innovation network.

- **Patient-Linked Precision Medicine:** HTS-driven drug sensitivity testing informed ZERO clinical decision-making, strengthening molecular tumour board recommendations for children with cancer
- **End-to-End Drug Discovery:** THINK program utilised HTS Facility for assay development (METTL1), large-scale compound screening (18,000 compounds across 2 targets), and lead progression (METTL5)—demonstrating movement from target identification to candidate compounds
- **Grant Success:** Supported 16 funding applications including NHMRC Ideas grants (x3), MRFF grants, TIA Pipeline Accelerator vouchers (x2 successful), NextSTEP Award, and Future Makers Challenge.
- **Capacity Building:** Trained 11 research staff in HTS design and execution; convened 3 User Group meetings and delivered 6 presentations to stakeholders.

Technology and Innovation Platform

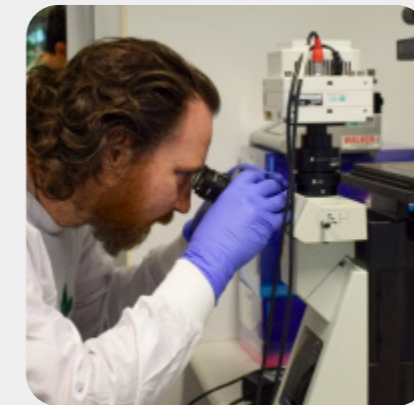
Chair: A/Prof Charley de Bock and Dr Rob Salomon

Enabling automated robotic systems and high throughput platforms for the acquisition and analysis of complex, information-rich functional data.

PROGRESS TO DATE

Capacity Building Program

Supported 4 NextSTEP (Scientific Training Exchange Program) grants and expanded across all Enabling Platforms and beyond, enabling unique skills generation through international expertise and technology access.



Community Engagement

Tech Connect Forum attracted >50 attendees from CCI and UNSW, featuring 2 commercial sponsors (BD and Miltenyi).

Training Workshop Success

Delivered integrated Enabling Platforms training workshop with >50 attendees, covering multiplexed imaging flow cytometry (IFC), epigenetics, and advanced flow cytometry applications.

Strategic Technology Access

Developing technology access programs modelled on VIB Tech Watch to enable early access to emerging technologies, positioning CCI for first-mover advantage through commercial partnerships.

Infrastructure Development

Contributed to ACRF ASPIRE/ACCEPT program equipment acquisition and facilitated MCCC flow cytometry capacity negotiations

Immuno-Oncology Enabling Platform

Co-Chairs: Dr Ernest Moles and Dr Klaartje Somers

To establish immune-oncology as a major new research capability of the Institute.

PROGRESS TO DATE

Technology Development

Established MAC-SIMA panel for spatial human immune profiling, OPAL spatial mouse immune panel (15-plex), and Cytek mouse immune profiling panel (40-plex), enabling comprehensive tumour microenvironment characterisation.

Biological Model Expansion

Expanded panel of immunocompetent syngeneic models and developed humanised mouse models and patient-matched humanised PDX models to support immuno-oncology research

Cross-Platform Integration

Established strategic alignment with Technology Innovation, Bioinformatics, Bioresources & Data, and FHTT platforms, creating integrated workflows for immune profiling and spatial analysis.

External Collaborations

Built partnerships with Peter MacCallum Cancer Centre, Telethon Kids Research Institute, University of South Australia, TRI/ University of Queensland, UNSW, and UTS.

Community Building: Established User Group with 2 meetings held in 2025, fostering knowledge exchange and collaboration.

LOOKING FORWARD

The Enabling Platforms have established themselves as integral to CCI's research ecosystem, delivering tangible impact through enhanced infrastructure, strategic collaborations, significant grant support, and comprehensive training programs. The platforms' collaborative approach and cross-platform integration demonstrate a model for enabling world-class paediatric cancer research. As the Institute transitions to the MCCC facility in December 2025, the platforms are well-positioned to expand their impact and support even greater scientific achievement.

Future Makers Challenge: Empowering Bold Ideas in Childhood Cancer Research

Children's Cancer Institute launched the Future Makers Challenge in 2025 to champion exactly the kind of research that defines our mission: innovative, collaborative, and unafraid to ask the difficult questions. With \$120,000 in funding available, this initiative represents more than just financial support. It embodies CCI's commitment to nurturing the next generation of scientific leaders whilst embracing intellectual risk-taking in pursuit of breakthroughs for children and young people with cancer.

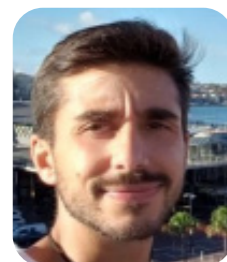
The Challenge explicitly seeks proposals that other funders might overlook: research that dares to fail in pursuit of transformative discoveries. By requiring cross-theme collaboration and engagement with our Enabling Platforms, the scheme reinforces that the most exciting advances in childhood cancer research emerge at the intersection of disciplines, where diverse expertise converges on shared challenges.

Three Innovative Projects

Following a rigorous two-stage selection process that included peer review by external scientific assessors and a consumer representative, three exceptional projects were selected. Each represents a unique Research Theme and collectively they exemplify the innovative spirit the Challenge was designed to foster.

1. Exploiting Cancer's Achilles' Heel

Dr Pablo Acera Mateos is pursuing an elegant approach to acute myeloid leukaemia, where approximately 20% of



patients harbour mutations in RNA splicing factors. These mutations correlate with devastatingly poor outcomes. His research capitalises on a remarkable vulnerability:

whilst individual splicing factor mutations can drive cancer, cells cannot tolerate multiple simultaneous perturbations to the spliceosome. By using small molecule splicing modulators to induce 'poison exons' specifically in mutant cells, Pablo aims to achieve synthetic lethality, turning the cancer's own genetic alterations into its undoing. This represents a promising avenue

for developing safer, more targeted therapies to replace the highly toxic chemotherapy currently used for AML.

2. Rethinking Immunotherapy Across the Lifespan

Dr Tom Mincherton's project tackles a critical yet understudied question in neuroblastoma treatment: why do developing immune systems respond differently to therapy? His research will establish an orthotopic immunocompetent high-risk neuroblastoma model in juvenile mice, comparing the tumour immune microenvironment and systemic immune responses during anti-GD2 monoclonal antibody therapy between young and adult animals. This work could fundamentally reshape our understanding of age-dependent immunotherapy efficacy, with direct implications for optimising treatment protocols in paediatric patients whose immune systems are still maturing.



3. Building Better Models for Better Treatments

Dr Anna Guller's project addresses a fundamental challenge in paediatric AML research: the lack of rapid, physiologically relevant in vitro models. Her multidisciplinary team is developing three complementary 3D culture platforms using extracellular matrix-based systems. These include innovative native tissue scaffolds derived from bone tissues, commercial gelatine-based photopolymerisable gels, and synthetic ECM-mimicking matrices for bioprinting. By incorporating spatially-complex magnetic

fields to enhance cell viability, this work will create powerful new tools for studying paediatric AML biology and testing therapeutic interventions in systems that better recapitulate the bone marrow microenvironment.



A Testament to Collaborative Science

What sets these projects apart isn't just their science, it's the deliberate collaboration behind them. Each brings together complementary expertise across CCI, with Enabling Platforms embedding cutting-edge technologies from day one to fast-track translation from concept to discovery.

The Future Makers Challenge is CCI's bold investment in people and ideas, empowering researchers at pivotal career stages to tackle high-risk, high-reward questions. Over the coming year, these projects will generate new knowledge, methodologies, and networks that resonate far beyond their immediate findings, demonstrating CCI's commitment to collaboration, ambition, and translation-focused impact.



Championing Technicians: Driving Global Standards at CCI

CCI proudly became the first Australian MRI to sign the internationally recognised Technician Commitment in 2024, affirming our pledge to elevate the role of technicians in science.

2025 HIGHLIGHTS

<p>TASK FORCE IN ACTION Regular Technician Commitment Task Force meetings shaping strategy</p>	<p>EMPOWERING MOBILITY First Technician Commitment Task Force Travel Award granted to Sarah Fox</p>
<p>YOUR VOICE MATTERS Inaugural Tech Connect Forum drew 50 attendees</p>	<p>GLOBAL PRESENCE Showcased CCI's Technician Commitment at ACS CYTO CONNECT international conference</p>

Through these initiatives, CCI is setting the benchmark for recognition, development, and influence of technical expertise, locally and globally.

ACRF Innovation Hub

Opening 2026 at Children's Cancer Institute

With transformative support from the Australian Cancer Research Foundation, Children's Cancer Institute will open the ACRF Innovation Hub in 2026, housing three world-leading research programs equipped with unprecedented technology.

The **ASpIRe Program** uses cutting-edge spatial multiomics platforms, including SomaScan, Australia's first of its kind, to map the immune landscapes of childhood brain tumours, sarcomas, and neuroblastoma at unprecedented resolution, revealing why immunotherapy succeeds in adult cancers but fails in children. The **ACCEPT Program** deploys advanced DNA methylation diagnostics, ALTE microdissection systems for drug sensitivity testing directly from tumour biopsies, RASTRUM 3D bioprinting to recreate tumours in their immune contexts, and pioneering SMIRFS technology that targets cancer-causing RNA rather than proteins—opening pathways to treat previously “undruggable” cancers. The **ACRF Child Cancer Liquid Biopsy Program** establishes Australia's most advanced non-invasive cancer monitoring capability through ultrasensitive INVAR detection achieving parts-per-million sensitivity, CellenONE cell pickers guaranteeing single-cell isolation at over 95% efficiency, and comprehensive single-cell sequencing platforms that can simultaneously profile DNA, RNA, and proteins from individual circulating tumour cells.

These programs have the potential to fundamentally transform outcomes for the approximately 1,000 Australian children diagnosed with cancer each year. The Hub will enable research into the identification of children at risk of cancer before symptoms appear, potentially allowing preventative interventions for children carrying inherited cancer mutations. Through non-invasive blood tests rather than repeated

invasive biopsies, doctors will be able to monitor treatment response in real-time, predict relapse months earlier than current methods, and track how tumours evolve and develop resistance to therapy. The spatial immune profiling will unlock immunotherapy for childhood cancers by revealing which children will respond and how to convert “immune cold” tumours into “immune hot” ones susceptible to treatment. Advanced tumour modelling will identify effective drug combinations for each child's unique cancer, expanding treatment options for children whose tumours currently have no targeted therapies. By comprehensively mapping tumour heterogeneity at single-cell resolution, the Hub gives researchers unprecedented insight into disease behaviour, enabling personalised treatment strategies that maximise survival whilst minimising lifelong side effects.

The ACRF Innovation Hub positions Australia as a global leader in paediatric cancer research, creating the world's most comprehensive analysis of childhood tumour immune



microenvironments and establishing international standards for paediatric liquid biopsy methodologies. The Hub's discoveries, spanning immunology, early detection, and precision diagnostics, will extend beyond childhood cancers to transform adult cancer care, with technologies and insights shared through partnerships with clinical sites across Australia and research collaborations worldwide.

Through ACRF's investment in world-class infrastructure and the integration of these programs with the Zero Childhood Cancer Program's national clinical trials network, Children's Cancer Institute advances towards its ultimate mission: ensuring survival for every Australian child diagnosed with cancer.

A new home for Children's Cancer Institute

The Minderoo Children's Comprehensive Cancer Centre (MCCCC) brings together leading clinicians, researchers and educators under one roof, with contemporary health facilities, laboratories and spaces for families to connect while navigating their healthcare needs.

In a first for Australia, childhood cancer research and the clinical care of children with cancer will integrate into one paediatric facility, accelerating the translation of research discovery into improved clinical practice.

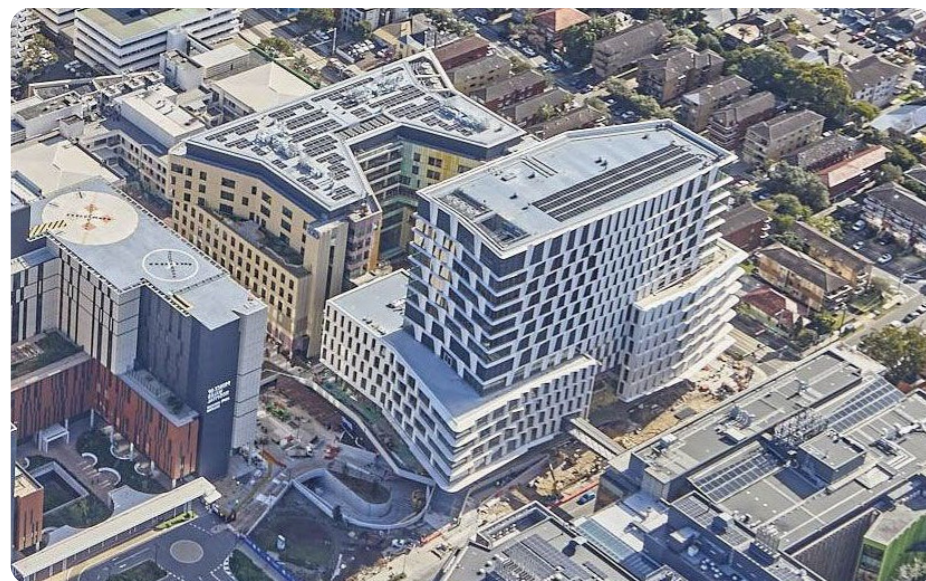
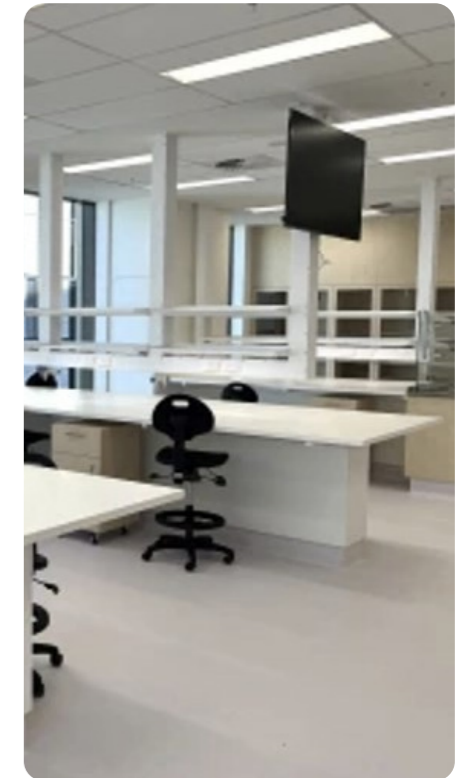
The MCCCC will be housed within the new hospital building and adjacent to the UNSW Health Translation Hub. It will be the new home for Children's Cancer Institute, with researchers working side-by-side with their clinical partners at the Kids Cancer Centre.

The Centre will include advanced laboratory spaces and deliver integrated, specialist cancer treatment, education and research programs, with the aim of transforming childhood cancer treatment and establishing itself as a global leader in paediatric cancer care.



Minderoo Children's Comprehensive Cancer Centre

Working together to end the burden of children's cancer



This is more than a building - it's a generational opportunity for research and clinical care to come together to deliver world-leading outcomes for children"

Michelle Haber



The Impact of Professor Michelle Haber on Paediatric Cancer Research



Over four decades, Professor Michelle Haber has fundamentally transformed paediatric cancer research and clinical care, establishing herself as one of the world's most influential figures in childhood oncology. Her contributions span ground-breaking discoveries in cancer biology, revolutionary clinical innovations, and the creation of research infrastructure that has positioned Australia as a global leader in precision medicine for children with cancer.

Pioneering Drug Resistance Research

Michelle's early work characterising the molecular mechanisms underlying therapy-related drug resistance in neuroblastoma laid the foundation for decades of translational advances. Her identification of the relationship between high expression of the multidrug transporter gene MRP1 and the malignant phenotype of neuroblastoma represented a watershed moment in understanding why some childhood cancers resist treatment. These studies provided the first definitive demonstration of clinical relevance of the MRP1 gene in solid tumours, resulting in a large international clinical study that confirmed the independent prognostic significance of MRP1 expression in neuroblastoma. This work established MRP1 inhibition as a potential new treatment strategy and opened an entirely new avenue of research that has influenced how researchers worldwide approach the challenge of treatment resistance.

Revolutionising Leukaemia Treatment Through Minimal Residual Disease Testing

One of Michelle's most profound clinical impacts came through her work with colleagues Professors Glenn Marshall and Murray Norris in developing and implementing molecular-based minimal residual disease (MRD) testing for children with acute lymphoblastic leukaemia (ALL). This PCR-based technology enabled detection of cancer cells that remain in the bone marrow at levels far below what traditional microscopy could identify, as few as one leukaemia cell amongst 10,000 normal cells.

The implementation of MRD testing fundamentally changed how clinicians stratify risk and guide treatment decisions for children with ALL. The impact was dramatic and immediate:

survival rates for children with high-risk ALL doubled from 35% to 70%. This breakthrough transformed MRD testing from an experimental approach into a routine clinical assay now performed at treatment centres across Australia and internationally. The work earned recognition as one of the ten best medical research programs in Australia by the National Health and Medical Research Council in 2012, and the team received the Cancer Institute NSW Premier's Award for Excellence in Translational Cancer Research.

Advancing Novel Therapeutics

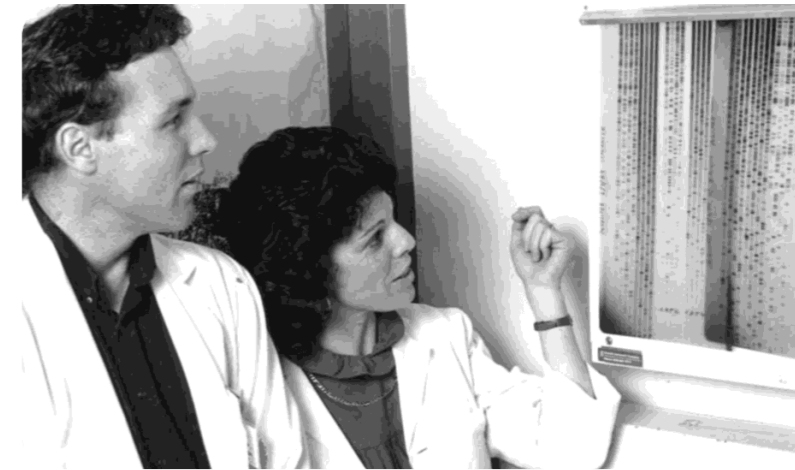
Michelle has pioneered multiple therapeutic approaches that have progressed to international clinical trials, targeting high-risk cancers where outcomes have historically been poor. Her work on polyamine inhibition therapy has led to completed trials in 15 children's hospitals and a current trial open in 120 hospitals internationally, with additional trials planned for neuroblastoma and brain tumours. She and her collaborators identified targeting of the chromatin modifier FACT using the novel drug CBL0137 as effective therapy for neuroblastoma, acute lymphoblastic leukaemia, and diffuse intrinsic pontine glioma, leading to clinical trials through the Children's Oncology Group, the largest children's cancer study group globally. Working in collaboration with local, national, and international colleagues, she played a leading role in advancing NAMPT inhibition therapy with OT-82 for refractory leukaemia and lymphomas to clinical testing.

The Zero Childhood Cancer Program: A Global Paradigm Shift

Perhaps Michelle's most ambitious and impactful contribution is the Zero Childhood Cancer Program (ZERO), which she conceived, championed, and brought to fruition as Australia's first national precision medicine program for children with cancer. Launched as a pilot in 2015 and expanded to a national clinical trial in 2017, ZERO represents one of the most comprehensive precision medicine programs for paediatric cancer in the world.



The program employs whole-genome sequencing, transcriptomic sequencing, and methylation profiling to identify the molecular drivers of each child's cancer, enabling clinicians to match treatments to the specific genetic and biological characteristics of individual tumours. ZERO's success has been transformative, and as a result, the Australian Government and the Minderoo Foundation committed \$67 million to expand the program, making it available to all Australian



children with cancer by 2023, the first time precision medicine has been universally accessible to every child diagnosed with cancer in any country worldwide. The program was selected as one of only six international programs featured in a NATO-commissioned review published in *Nature Cancer Reviews*, and Michelle was invited to present ZERO at the American Association for Cancer Research's Presidential Select Symposium in 2020, a rare honour reflecting the program's global significance. Beyond immediate clinical impact, ZERO is widely regarded as the leading child cancer precision medicine program globally. In 2025, ZERO received an additional \$112.6 million investment from the federal government to continue operations and expand to all Australian young adults aged 19-25 with paediatric-type cancers.

Building Research Infrastructure and Leadership

Under Michelle's executive leadership since 2003, Children's Cancer Institute has more than quadrupled in size and evolved from a relatively unknown group into the largest children's cancer research facility in the region and an internationally recognised centre of excellence. Through her vision and advocacy, she helped drive the development of the Minderoo Children's Comprehensive Cancer Centre, opened in 2025, set to integrate world-class research and clinical care under one roof.

International Recognition and Influence

Michelle's contributions have earned extraordinary recognition: Member of the Order of Australia (2007), named as one of Australia's 25 "True Leaders" by the Financial Review (2007), Honorary Doctor of Science from UNSW (2008), inaugural Fellow of the Australian Academy of Health and Medical Sciences (2015), election to the Australian Academy of Science (2022), the Sidney Sax Medal for outstanding contributions to Australia's healthcare system (2023), and the Lifetime Achievement Award from the Advances in Neuroblastoma Research Association (2023). Just recently in 2025, she was awarded the prestigious Royal Society NSW, James Cook Medal and the Lemberg Medal from the Australian Society for Biochemistry and Molecular Biology.

Michelle's impact extends far beyond individual discoveries or awards. She has fundamentally changed how paediatric cancer is understood, diagnosed, and treated not just in Australia, but globally. Through her combination of rigorous science, translational vision, and unwavering commitment to improving outcomes for children with cancer, she has created a legacy that will save countless lives for generations to come.



Welcoming our new Executive Director!

Brief Biography

Professor Louis Chesler is an internationally renowned clinician-researcher who has dedicated his career to discovering and translating new treatments for children with cancer.

Born in South Africa, he completed his scientific and medical training in the United States, earning his MD and PhD from Northwestern University Medical School in Chicago, and his BSc (Honours) from the University of Wisconsin-Madison.

He worked as an Intramural Fellow at the National Cancer Institute (NCI), Bethesda, before joining the University of California, San Francisco, as a paediatric oncology consultant whilst leading his neuroblastoma research program.

Since 2007, Professor Chesler has served as Head of the Centre for Paediatric Oncology Experimental Medicine at The Institute of Cancer Research (ICR), London, one of the world's premier cancer research institutions, where he is also Endowed Professor of Paediatric Cancer Biology and Honorary Consultant at the Royal Marsden Hospital.

Strengthening the Institute's future

World-Leading Scientific Expertise: Louis is recognised globally as a pioneer in targeting the MYCN oncogene in paediatric solid tumours, particularly neuroblastoma, medulloblastoma, and rhabdomyosarcoma. His groundbreaking work on therapeutic strategies to destabilise MYCN protein has opened new avenues for treating high-risk childhood cancers. His research on PI3K/mTOR pathway inhibitors and their ability to target MYCN has directly informed clinical trial design.

Unique Clinician-Scientist Perspective: As both a practising paediatric oncology consultant and a laboratory researcher, Professor Chesler brings the rare ability to understand cancer from both the bedside and the bench. This dual perspective ensures research is always grounded in clinical reality and patient need, exactly the translational approach CCI champions.

Track Record in First-in-Child Therapeutics: His Centre at ICR is renowned globally for its breakthroughs in first-in-child therapeutics and genomic-driven precision medicine trials. This expertise is precisely what CCI needs as it enters the MCCCC era, where bench-to-bedside translation will be accelerated.

International Leadership and Networks: Louis is part of the Cancer Grand Challenges PROTECT team (a \$125 million international initiative), leads the Stratified Medicine Paediatrics 2 program, and is a member of the Cancer Research UK Convergence Science Centre. These connections will bring invaluable international partnerships and funding opportunities to CCI.

Perfect Alignment with CCI's Mission: Louis' vision perfectly aligns with CCI's strategy. He has stated his goal of developing "a one-a-day pill that would be free of side-effects and very effective against children's cancer", echoing CCI's commitment to finding kinder, more effective treatments. His focus on understanding childhood cancers as developmental diseases also aligns with CCI's research philosophy.

Strategic Timing: Louis' appointment coincides with CCI's move into the MCCCC, creating a unique opportunity to build integrated programs between research and clinical care from the ground up, something he's experienced at the ICR/Royal Marsden partnership.

Drug Development Expertise: At a time when CCI is advancing initiatives like THINK drug development, Louis brings unparalleled expertise in taking novel therapeutics from preclinical models through to clinical trials specifically for paediatric populations.



Global Recognition: The international search that led to his appointment demonstrates CCI's ambition, and his acceptance shows his confidence in CCI's potential. As UNSW Provost Professor Vlado Perkovic stated, "This is an exciting new chapter for one of Australia's most impactful medical research organisations."

Professor Michelle Haber's endorsement is telling: "I have hoped for many years that we would be able to recruit Lou to Children's Cancer Institute, and I couldn't be more delighted... I have no doubt that our impact will not only continue but accelerate."

This appointment signals CCI's commitment to remaining at the absolute forefront of paediatric cancer research globally, with a leader who combines scientific excellence, clinical wisdom, and a proven track record of translating discoveries into better outcomes for children with cancer.

Health Impact

ZERO in 2025

1000 enrolments high-risk, relapsed, rare and undiagnosable cancers

3000+ children and young people enrolled (2017- today)

2023-ONGOING >2000 enrolments All children with cancer irrespective of cancer type, stage or risk

International Reach: 14 treating centres/hospitals across Australia (12) & New Zealand (2).

In October 2025, the \$112.573 million Commonwealth Grant Agreement for ZERO was fully executed

A national consultation survey was recently launched to gather input from clinical stakeholders, to effectively expand access to adolescents and young adults (AYAs) aged 19–25 with paediatric-type cancers

ZERO2 at national scale: enrollment rate sustained at ~66 children/month with target of 750/year surpassed in 2024; clinical turnaround **under 12 weeks** from enrollment to report delivery to treating clinician.

Equity progress: Aboriginal and Torres Strait Islander participation ~6.4% of ZERO2 enrollments (Nov 2023–Jun 2025) with culturally safe governance plans underway.

Preclinical testing fills clinical gaps: 15 patient samples tested (Jan–Jun 2025); **90%** revealed cancer specific vulnerabilities, including **40%** of cases with no recommendations from genomics alone.

Liquid biopsy (ctDNA) capability maturing: >707 samples processed and >180 patients analysed; policy framework finalised.

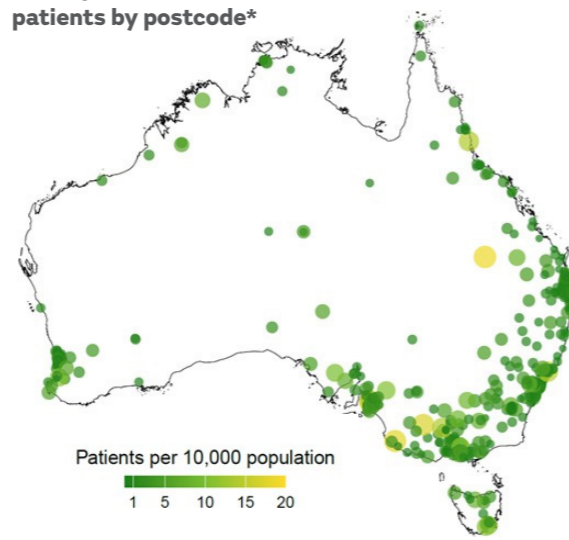
International Gold Standard: ZERO's pipelines have been adopted by seven countries participating in the ITCC Hopp initiative for conducting whole-genome sequencing for paediatric cancer precision medicine, serving as the gold standard for global data harmonisation.

Funding to support expansion and continuity of Zero Childhood Cancer Program

In March 2025, it was announced that the ZERO Childhood Cancer Program will receive a \$112.6 million investment from the Australian Government to extend and expand so that more children and young people can benefit from the latest in scientific and clinical understanding.

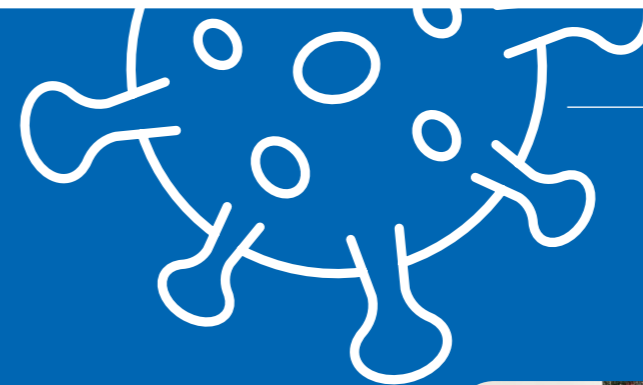
Led by Children's Cancer Institute and Kids Cancer Centre at Sydney Children's Hospital, Randwick, and involving all of Australia's children's hospitals, the funding will ensure ZERO can continue to support this world first delivery of cutting-edge cancer care to all children with cancer (0-18 years), and expand the program to be available to many young people aged 19 to 25 with paediatric type cancers. The expanded program is expected to support an additional 300 young Australians with cancer each year, totalling approximately 1300 children and young people annually who will have access to ZERO's comprehensive precision medicine platform.

Per capita distribution of ZERO2 patients by postcode*



Nowhere else in the world do children with cancer have the opportunity of benefiting from a precision program of this depth and impact. ZERO is showing just what's possible when you combine cutting-edge research and technology with a multidisciplinary team approach to drive clinical care.

Professor Michelle Haber



Clinical One Delivers National Capability for Childhood Cancer Research

The ZERO2 electronic data capture (EDC) system has been successfully rebuilt on Oracle's Clinical One platform - now live across all 11 paediatric oncology sites in Australia and New Zealand. This upgrade replaces the legacy system, enabling streamlined enrollment, migration of 1,900 participant records and 520,000 data points, and delivering:



FASTER WORKFLOWS
Integrated notifications and smart form logic.



IMPROVED DATA INTEGRITY
Harmonised, high-quality data across sites.



REDUCED MANUAL ENTRY
Less duplication, more efficiency.

With new enrollments underway, the next phase focuses on migrating existing data, supported by rigorous testing and comprehensive site training. This achievement reflects an extraordinary collaborative effort by the ZERO team, KOALA, Kids Cancer Centre, and Oracle partners.

One national system, stronger data quality, and a better experience for clinical teams.



Update on LEVI's CATCH

- Levi's Catch is the first clinical trial of its kind in Australia, or indeed anywhere outside of the U.S.
- It is based on a type of immunotherapy called chimeric antigen receptor (CAR) T-cell therapy
- The trial uses CAR-T cell therapy to genetically modify a patient's own immune cells in a laboratory to teach them to target and attack the tumour. The hope is once reinfused into the patient, these immune cells will have the ability to scan and destroy harmful cancer cells without damaging the most other healthy cells. CAR is given with bevacizumab.
- 12 patients currently enrolled, with successful manufacture of CARs.
- Early data show potential differential cytokine profiles between responders and non-responders

Integration of germline findings

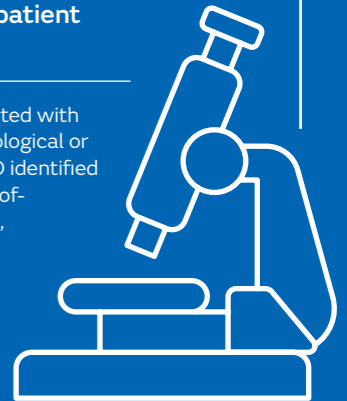
Direct association of SMARCAL1 in osteosarcoma

Our researchers have used clinical data from ZERO to reveal that SMARCAL1 is directly linked to osteosarcoma (and not other cancer types) - a clinically critical distinction for family counseling and risk assessment.

From these findings, three families have already received genetic explanations for their child's osteosarcoma, demonstrating ZERO's immediate translational impact on patient care.

Dual diagnoses transforming patient care

Two children (aged 6–9 years) presented with cancer alongside unexplained immunological or neurodevelopmental symptoms. ZERO identified pathogenic DIAPH1 and SMAD4 gain-of-function variants as the genetic cause, enabling targeted treatment of their underlying conditions and profoundly improving quality of life beyond their cancer care.



Clinical Trials

In 2025, CCI researchers have contributed to **>26** active clinical trials

OPTIMISE Trial Expands

Second Treatment Arm Opens

Launched in July 2024, the OPTIMISE trial is Australia's first childhood cancer platform trial, developed and led in partnership with Canada's C17 Council and PROFYLE program. Now active at all nine Australian paediatric oncology centres and five Canadian sites, OPTIMISE is transforming how children, adolescents and young adults with high-risk cancers are treated.

Why it matters

Adaptive design

Multiple treatment arms run simultaneously, matching patients to therapies based on their tumour genetics.

Goal

Broaden treatment options and improve outcomes for children, adolescents, and young adults with advanced solid tumours, brain tumours, or lymphomas.

Treatment arms

ARM B (2025)

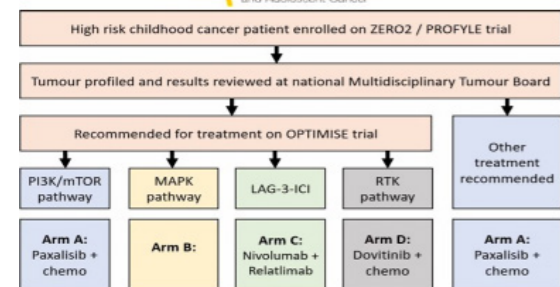
Paxalisib + chemotherapy for PI3K/AKT/mTOR pathway alterations.

ARM C

Dual immune checkpoint inhibitors (nivolumab + relatlimab) for tumours with high immune cell infiltration or replication repair deficiency.

Immune checkpoint inhibitors have revolutionized adult cancer care. CCI researchers have shown that ~31% of paediatric high-risk patients are T-cell infiltrated (Mayoh et al, Genome Medicine, 2023).

By targeting paediatric patients most likely to benefit, OPTIMISE aims to bring this breakthrough to childhood cancer treatment.

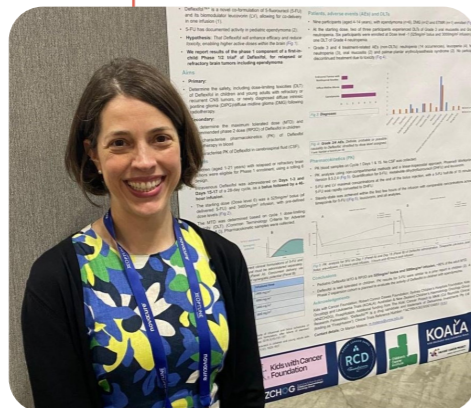


Completion of Phase 1 DART TRIAL:

Establishing Safety in Children

A first-in-child Phase 1 trial evaluated **Deflexifol**, a novel co-formulation of 5-fluorouracil (5-FU) and leucovorin, in children with relapsed or refractory brain tumors, including ependymoma, diffuse midline glioma (DMG) and Embryonal Tumor with Multilayered Rosettes (ETMR).

- 9 children (ages 4–14)
- Find the safest dose for kids
- 3-day infusion cycles, rolling dose escalation
- SAFE DOSE**
525 mg/m² bolus + 3000 mg/m² in-fusion x(=88% of adult dose).
- TOLERABILITY**
Well tolerated; main side effects were mouth sores and low white cell counts. No treatment stopped due to toxicity
- PHARMACOKINETICS**
Similar to adults:
- Peak drug levels right after bolus
- Steady levels maintained during 46-hour infusion
- NEXT STEPS**
Phase 2 expansion to test



Left: Dr Marion Mateos, Clinician Scientist and Paediatric Oncologist presenting these data at the Society for Neuro-Oncology Conference, Hawaii

Informing Decision Making

Advocacy Priorities (2025)

Our 2025 advocacy priorities focused on:

Raising awareness of the Minderoo Children's Comprehensive Cancer Centre (MCCCC) - its purpose, potential, and future impact

Enhancing paediatric drug access and discovery.

Expanding and sustaining the ZERO Childhood Cancer Program.

Improving the research funding ecosystem.

Many of these priorities were not initially on the government's agenda but have since gained attention and traction thanks to our advocacy efforts.

Government Engagement

In the past year, we have undertaken approximately 160 engagements with bureaucrats and parliamentarians through meetings, site visits, and participation in CCI events such as the Diamond Ball.

During Childhood Cancer Awareness Month (CCAM), awareness ribbons were distributed to all NSW Parliamentarians, many of whom wore them in Parliament to show support.

Several MPs and Senators have since acknowledged CCI's work and the broader impact of childhood cancer in parliamentary proceedings.

Our researchers have played an active role in these efforts, contributing to messaging, attending meetings and lab tours, and informing submissions to government, which has strengthened the credibility and impact of our advocacy.



Professor Michelle Haber leading a Lab Tour at Children's Cancer Institute with Senator Jessica Collins, Federal Senator for NSW



A/ Prof. Antoine de Weck, Group Leader of Computationally Enabled Drug Discovery, who is dedicated to discovering and developing safer, more targeted therapies for children with cancer, alongside Maryanne Stuart MP, Member for Heathcote.

2025 Advocacy and Policy Highlights

In 2025, CCI contributed feedback to 20 government consultations, including legislative reforms, draft frameworks and strategies, strategic examinations, and discussion papers, with many of our recommendations reflected in final outcomes.

Key submissions included:

- Draft National Framework for Genomics in Cancer Control
- Strategic Examination of Research and Development
- National Health Genomics Policy Framework
- Productivity Commission Inquiries – Interim Reports
- Draft National Health and Medical Research Strategy

- Possible Association to Horizon Europe
- Future NSW Cancer Plan
- Future Childhood and AYA Cancer Roadmap
- Medical Research Support Program Review

CCI's submission to the Equitable Access to Diagnosis and Treatment Inquiry directly contributed to the Federal Government accepting a recommendation to fund the ZERO Childhood Cancer Program.

CCI established a strategic partnership with Cancer Australia to support delivery of the Australian Cancer Plan.

Informing Decision Making

Our researchers are actively engaged in **>44** different strategic panels or committees

(e.g., Randwick Health & Innovation Precinct -Rare Diseases NSW Committee; Childhood and AYA Cancer Roadmap Expert Reference Group; NSW Cancer Plan consultation committee; Inaugural AACR Paediatric Cancer Progress Report Steering Committee; Australian Genomics National Steering Committee; Cancer Australia Genomics Working Group, etc.)

Our researchers have provided expert advice in **>21** advisory boards

(e.g., Chair, MRFF Brain Cancer Mission's EAP; ProCan Scientific Advisory Board, Luminesce Alliance Board, Inventia Life Science Scientific Advisory Group, Australian Centre for RNA Therapeutics in Cancer Scientific Advisory Group etc.)

Right: A/Prof. Ness Tyrrell and Dr Richard Mitchell (Director of the Kids Cancer Centre with Senator Deborah O'Neill (Federal Senator of NSW, and Co-Chair, Parliamentary Friends of Cancer Care



Economic Impact

KAT6 Inhibitor Program Contributing to a Breakthrough in Cancer Therapeutics

Children's Cancer Institute contributed to a landmark Australian drug discovery success story that has reached Phase 3 clinical trials with Pfizer Inc. The KAT6 inhibitor program, originating from pioneering research at the Walter and Eliza Hall Institute and developed by the Cancer Therapeutics Cooperative Research Centre (CTx), to which CCI was a member from 2014 - 2020, represents a first-in-class approach to treating cancer by targeting the histone lysine acetyltransferase enzyme KAT6A/B. CCI's contributions involved pre-clinical screening to identify potential paediatric cancer indications.

In 2018, the program was licensed to Pfizer for US\$14.2 million upfront, with potential milestone payments up to US\$460 million and royalties on future product sales. Following promising Phase 1 results, Pfizer's investigational drug PF-07248144 commenced a Phase 3 clinical trial in September 2025 (KATSIS-1) for hormone receptor positive, HER2-negative metastatic breast cancer, aiming to enrol 400 subjects across international sites including several Australian hospitals.

Professor Ian Street (pictured), previously CTx Chief Scientist, and now Director of CCI's Drug Development Program, Therapeutic Innovation for Kids (THINK), highlighted the collaborative nature of this achievement: "In the early 2000s at Walter and Eliza Hall Institute (WEHI), Anne Voss and Tim Thomas made foundational discoveries about KAT6A, a protein that is important for controlling gene expression during development and growth of some blood cancers. Many CTx research and industry partners—Monash Institute of Pharmaceutical Sciences, SYNthesis Med Chem, Peter MacCallum Cancer Centre, WEHI, CSIRO, Griffith University, St Vincent's Institute of Medical Research, and the Children's Cancer Institute, along with Pfizer, have worked together to develop a new drug that targets KAT6. This is a deeply inspiring story of collaboration in Australia's medical research sector."

This program exemplifies how CCI's expertise in paediatric pre-clinical screening can contribute to broader cancer drug development efforts with potential global impact. Looking forward, CCI is excited to explore potential applications of KAT6 inhibitors in paediatric cancer indications, particularly considering recent evidence demonstrating that catalytic inhibition of



KAT6/KAT7 enhances the efficacy of menin inhibitors and overcomes resistance in MLL-rearranged leukaemia—a particularly aggressive subset of paediatric acute myeloid leukaemia that frequently relapses after standard therapy.



I would like to congratulate the visionary and talented Australian scientists and clinicians who contributed to the discovery and development of PF-07248144, and of course, share our sincere gratitude to Pfizer for backing this potential cancer therapeutic so quickly into a Phase 3 Clinical Trial."

Professor Ian Street

Commercialisation Seed Fund

In January, CCI's Business Development team launched CCI's first Commercialisation Seed Fund round. The purpose of this fund is to support advanced research projects and innovations with commercial potential that require focused and strategic Proof-of-Concept support. The aim is to de-risk CCI projects and increase chances of commercial success. We had 6 EoI applications from our researchers, and 3 were selected to progress to full application. An external panel of experts with experience in commercialisation provided scores and feedback on the applications and 2 teams were awarded \$25,000 each for their projects



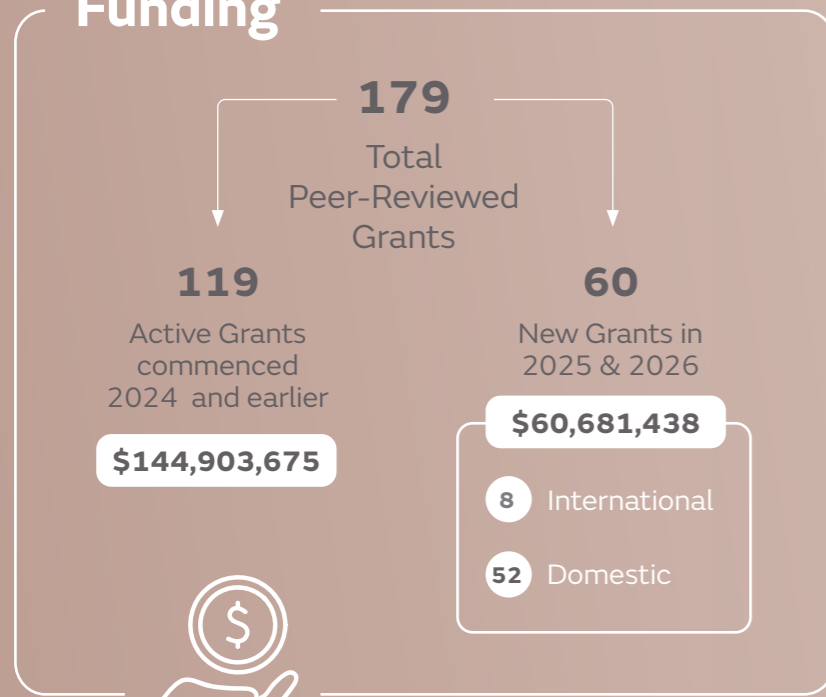
Dr Kevin Wang, Drug Discovery Officer from THERapeutic INnovations for Kids (THINK) group



Dr Shi Yan Lee, Postdoctoral Scientist from the Computationally Enabled Drug Discovery group

Economic Impact

Funding



Business Development Team Highlights

New Intellectual Property (IP) Policy

A new and improved IP Policy is an integral part of the Institute's goal to maximise our impact on patient outcomes. It will strengthen the Institute's potential to commercialise its discoveries, as well as to attract, retain and incentivise the brightest and best researchers to innovate and generate novel IP.



Commercial IP License with Saphetor

CCI has finalised a commercial IP license with **Saphetor**, unlocking worldwide access to SpliceVarDB—a powerful database developed by our computational biology team. Saphetor will integrate SpliceVarDB into **four commercial products** used by customers worldwide, significantly extending the global impact of CCI-developed data assets.



CCICB/
SpliceVarDB

An online database of variants functionally demonstrated to affect (or not affect) splicing.



Accelerating Industry Partnerships

Industry engagement at CCI has accelerated significantly, with growing recognition of our expertise, high-value datasets, unique disease models, and the clinical translation pathways enabled through the ZERO program. CCI is currently in active discussions with **14 global industry partners**, spanning co-development and collaborative research, preclinical testing, contract research, asset licensing, venture capital engagement, and accelerated drug discovery.



4 contract research engagements are currently underway, with several additional opportunities progressing under confidentiality agreements.

Collectively, these achievements directly advance CCI's strategy to translate research into clinical impact, leverage our specialised capabilities to enable the use of targeted therapies for paediatric patients, and deliver meaningful commercialisation outcomes.

Social Impact

CCI researchers don't just work in the lab, they step into the community to create impact. From the glamour of the Diamond Ball to the grit of 86K for a Cure, and the ideas sparked at UNSW's One Big Idea, our scientists are leading conversations and driving breakthroughs - because curing kids' cancer takes all of us.

19 Lab Tours

for 110 Visitors led by

25 Researchers from January – August 2025*

90 Occasions of Public Engagement through seminars, fundraising events, and community outreach activities

e.g. Volunteering at CCI Fundraising Events – Diamond Ball, 86K Step Out for Cancer; Invited Presentations at Donor Events – Robert Connor Dawes Foundation, The Kids Cancer Project Luncheon; etc,

* Lab Tours were halted from August 2025 due to the transition into the MCCCC



Raising Awareness, Driving Impact

Brain tumour researcher Dr Aaminah Khan and Clinician Scientist and Paediatric Neurooncologist Dr Neevika Manoharan were invited to speak at the Robert Connor Dawes Foundation's NSW Connor's Golf Classic, an event uniting families, clinicians, researchers, and supporters to improve outcomes for children with brain cancer. The Foundation's commitment goes beyond events: it funds travel grants that open doors for emerging talent, including one awarded this year to CCI PhD student Philipp Graber, enabling young researchers to share their work on a global stage.



Big Ideas, Bigger Impact

At a sold out public event, hosted by UNSW's Centre for Ideas - One Big Idea at the NSW State Library, CCI's Prof. Maria Kavallaris showed how nano "GPS" drug carriers could spare kids the toxic side effects of chemotherapy, while Dr. Alexis Minchaca Acosta revealed how new blood-brain barrier models can unlock treatment for brain tumours. In front of a packed audience and policymakers, their talks turned complex science into clear, hopeful narratives, deepening public trust, inspiring support, and accelerating the path from lab discovery to patient impact.



Not surprisingly, our brain is incredibly well protected. There is a structure called the blood-brain barrier, that acts as border security. It is like having a locked door with no key. To make that key, that drug, we first need a really good testing system that recreates the lock."

Dr Alexis Minchaca Acosta



Driving Change Through Connection

In September, Neuroblastoma Australia hosted Sienna's Frangipani Gala Dinner, a sold-out event honoring Sienna's legacy and rallying support for childhood cancer research. CCI researchers Prof. Michelle Haber, Prof. Murray-Norris, and A/Prof. Jamie Fletcher inspired a packed room with insights into the future of childhood cancer treatment. Their message of hope helped raise an incredible \$123,000, fueling research that will change outcomes for children with neuroblastoma. This is social impact in action: science connecting with hearts and communities.



Moving Together for Kids' Cancer

On November 9, CCI students and researchers stepped out with Tour de Cure to raise awareness and funds for childhood cancer research. A total of \$302,919 was raised by the community to support the Minderoo Children's Comprehensive Cancer Centre (MCCCC).



Turning Insight into Impact

A lab tour conducted in June 2025 led by A/Prof Maria Tsoli (far left), a Senior Scientist working on brain tumours, alongside Anne Johnston, gave Kerr Neilsen a Senior Scientist and Julian McCormack a firsthand look at our cutting-edge work. The result? A \$250,000 donation to CCI's Brain Tumour Group, fueling research that brings hope to children with the most aggressive cancers. This is the power of engagement: when science inspires generosity, lives change.

Looking Forward

Building on Excellence to Transform Childhood Cancer Care

The 2025 Research Impact Report reflects a year of extraordinary achievement during a period of significant transformation for Children's Cancer Institute. As we mark the conclusion of Professor Michelle Haber AM's distinguished 22-year tenure as Executive Director, we do so with immense gratitude for her visionary leadership that has positioned CCI as a global leader in paediatric cancer research.

This year's achievements demonstrate the strength and depth of our research enterprise. Our researchers have advanced knowledge across every domain, pioneering new precision oncology platforms, establishing innovative pre-clinical models, uncovering novel therapeutic targets, and developing computational tools that are transforming genomic interpretation worldwide. With high-impact publications, multiple clinical trials, and groundbreaking discoveries in cancer biology and therapeutic development, we have strengthened our position at the forefront of childhood cancer research.

Our impact extends beyond laboratory and clinic. Through sustained government engagement and policy contributions, we have influenced national frameworks. Our advocacy has strengthened the research funding ecosystem and enhanced the policy environment for paediatric cancer research.

As we welcome Professor Louis Chesler as our incoming Executive Director, we embark on a new chapter with exciting opportunities to strengthen and expand our impact. The Minderoo Children's Comprehensive Cancer Centre will unite research and clinical care under one roof for the first time in Australia, whilst the ACRF Innovation Hub will provide access to world-leading technologies. These infrastructure investments, combined with the major expansion of the ZERO Program now accessible to all Australian children with cancer, position us to accelerate the translation of discovery into improved outcomes for patients.

None of this would be possible without the support of our funders, philanthropic partners, clinical collaborators, government stakeholders, and the families who entrust us with their hope. To our researchers, students, and professional staff: thank you. Your commitment to scientific excellence and translational impact drives us ever closer to our vision.

As we look ahead, we do so with renewed purpose and clear direction. The foundations laid in 2025, in research discovery, clinical translation, infrastructure development, and stakeholder engagement, provide the platform for even greater impact in the years ahead.

Together, we are transforming the future for children with cancer. Together, we will save the lives of all children with cancer and improve their long-term health.



**We will cure every child of cancer.
It's not if, it's when.**

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