THE KIDS' CANCER PROJECT

The Kids' Cancer Project Symposium Abstracts

Abstracts have been categorised under the key research pillars of The Kids' Cancer Project – Discover, Support, Translate and Build.

To learn more about the pillars themselves, please click here.

DISCOVER

SUPPORT

TRANSLATE

Dr Aaminah Khan

Children's Cancer Institute

Funding provided via Col Reynolds Research Fellowship

Polyamine Pathway Blockade Sensitises MYC-Driven Medulloblastoma to Chemotherapy

The project

This project investigates the therapeutic potential of targeting the polyamine metabolic pathway in MYC-driven medulloblastoma - the most common malignant brain tumour in children. Building on previous findings in DIPG, we explore inhibition of the polyamine pathway as a strategy to suppress tumour growth and enhance chemotherapy efficacy.

The problem

Children with MYC-driven medulloblastoma face poor outcomes and limited treatment options, especially at relapse. Despite aggressive therapy, survival rates remain low and long-term side effects are common.

There is an urgent need for safer, more effective treatments that target the unique biology of high-risk medulloblastoma and improve outcomes for young patients.

The why

Brain tumours are the leading cause of cancer-related death in children. Medulloblastoma, in particular, can rapidly spread through the brain and spinal cord and disproportionately affects young children during key stages of development. Survivors often experience debilitating side effects due to the toxicity of current therapies.

Novel, targeted treatments are urgently needed to improve survival while minimising harm to the developing brain.

Our approach

We used gene expression data from the ZERO childhood cancer platform to identify polyamine dysregulation in medulloblastoma, then applied a dual-targeting strategy to block both polyamine synthesis (via DFMO) and transport (via AMXT 1501).

Our approach is bold in its combination of metabolic inhibition with chemotherapy, designed to selectively impair tumour DNA repair and sensitise cells to irinotecan. We've used in vitro synergy assays, RNA-seq, apoptosis profiling, and an orthotopic in vivo model to demonstrate therapeutic potential. This translational pipeline is informed by ongoing clinical trials and driven by cross-disciplinary collaborations.

Our progress

- Identified overexpression of polyamine regulators in medulloblastoma using the ZERO platform
- Demonstrated potent synergy between DFMO+AMXT 1501 and SN-38 (active metabolite of irinotecan) in MYC-amplified medulloblastoma cell lines
- RNA-seq revealed suppression of DNA repair pathways following polyamine blockade
- In vivo, dual therapy significantly extended survival; triple therapy (with irinotecan) achieved complete tumour eradication in 7/8 mice
- Histology confirmed absence of proliferative tumour cells in long-term survivors
- Findings support ongoing early-phase clinical trials evaluating this therapeutic combination in paediatric CNS tumours

What's next

Key next steps include validating efficacy in more patient-derived xenograft models and exploring combination timing and dosing strategies.

We welcome collaboration from clinicians, pharmacologists, and translational researchers to help refine trial design and expand this work into other paediatric brain tumour types.

A/Prof Emmy Fleuren

Children's Cancer Institute

Funding provided via Col Reynolds Research Fellowship

Accelerating the Discovery and Clinical Translation of Targeted Therapeutics for Young Sarcoma Patients

The project

Better, less toxic treatments for children with an aggressive and difficult-to-treat type of cancer called sarcoma are urgently needed. This project aims to find these treatments and make them a reality for children who are currently missing out.

The problem

Children with a difficult-to-treat type of cancer called sarcoma urgently need better, less toxic treatment options. Findings those treatments are, however, incredibly challenging. While many modern cancer therapies are designed to target specific changes in the tumour's DNA (called genetic mutations) that drive the growth of the cancer, most young people with sarcoma do not have these targetable, "druggable", mutations. This means we must look beyond genomics investigations to find new, targeted treatments for these young patients.

The why

Unfortunately, even with broader screening strategies, it remains very difficult to provide a confident and robust therapeutic recommendation for young people with sarcoma. The ZERO Childhood Cancer program for example, which is Australia's national precision medicine platform aimed to identify personalised therapies for children with cancer, comprehensively investigates every child's tumour with so-called molecular genomics and transcriptomics, and, when possible, by testing novel drugs on patient's tumour cells grown in a dish in the lab.

Although ZERO's testing platform is comprehensive and has helped many patients, most sarcoma patients still miss out on receiving a targeted drug.

Our approach

To tackle this, I designed a new program, aimed to both accelerate the discovery of new and better targeted drugs, plus bring those discoveries closer to patients. My discovery platform combines three innovative approaches to study sarcoma in ways no-one else does. It includes state-of-the-art 'phosphoproteomics', to pinpoint those drug targets that are truly activated, and investigates underexplored molecular and drug data from ZERO.

To build the most compelling data for clinicians, we next test if, and why, selected drugs affect sarcoma growth in our lab through a robust 'functional validation platform'. This bench-to-bedside childhood sarcoma program is globally unique.

Our progress

While this program started just over three months ago, I note the following. Presented at the biennial national Cell Signalling and its Therapeutic Implications (CSTI) meeting in Cape Schanck in May this year on "Phosphoproteomics in precision medicine: a promising target discovery platform for paediatric sarcoma", to 1) increase awareness, engagement and excitement on the phosphoproteomics part of my program, 2) strengthen and forge new partnerships, and 3) discuss and learn about the latest cell signalling and phosphoproteomics technologies and data interrogation options. This enabled me to determine the optimal sarcoma cohort for our next phosphoprofiling effort, plus learn how to get an even better understanding of sarcoma biology with new data interrogation methodologies. Performed initial interrogation of ZERO's data, revealing several un(der)explored, yet promising novel therapeutic avenues for young sarcoma patients that are currently not clinically acted upon.

What's next

My next plans essentially encompass performing the remainder of my Col Reynolds program. Through a cutting-edge multilateral discovery platform coupled to a robust validation framework, I aim to; 1) pinpoint the best drug targets and, 2) drive the laboratory research to translate these findings to the clinic, to truly make new drugs a treatment reality for young sarcoma patients. Input and advice are always welcome.

One thing I am curious about, is what (other) type of data would you (clinicians, community, or other researchers) like to see before moving new drugs to the clinic? I also very much welcome new collaborations to further advance sarcoma research together.

Dr Kenny Ip

Children's Cancer Institute

Funding provided via Col Reynolds Research Fellowship

Identifying a novel low-toxicity therapy for high-grade glioma patients to improve the post-treatment quality of life

The project

Mapping tumour-projecting neurons in incurable paediatric high-grade gliomas (pHGG) to identify cancer-promoting neural circuits and develop targeted, low-toxicity treatments that preserve neurological function and quality of life for young patients facing this devastating brain cancer.

The problem

H3-G34R/V and H3 K27M pHGG are among the deadliest childhood brain cancers, with dismal survival rates and no cure available. Current treatments rely on high-dose radiation therapy that offers only palliative relief while causing devastating neurotoxic side effects, including neurocognitive impairment that severely impacts young survivors' quality of life and developmental potential. These aggressive tumours exploit neural circuits to drive treatment resistance and tumour growth. The critical unmet need is developing targeted therapies that effectively kill cancer cells without the neurotoxic side effects that rob children of their cognitive abilities and long-term neurological function.

The why

pHGG have five-year survival rates below 2%, with most patients dying within 12 months of diagnosis. These brain tumours are the leading cause of cancer-related death in children. The limited clinical trials available globally offer few treatment options beyond high-dose radiation therapy, which provides only palliative care. The tumours are highly aggressive and resistant to conventional treatments. Current therapies cause significant neurotoxic side effects while failing to extend survival meaningfully. The lack of effective therapeutic options represents a critical unmet medical need in paediatric oncology, with virtually no curative treatments available for these devastating cancers.

Our approach

Our methodology represents the first systematic platform combining neural circuit analysis with precision medicine for paediatric brain cancer. We use retrograde circuit tracing to map tumour-projecting neurons, then employ viral-genetic DREADDs technology for circuit manipulation—allowing us to selectively activate or inhibit neural pathways driving tumour growth. This combines with our TRAP RNA sequencing to identify cancer-promoting factors and drug screening of over 2,000-compounds. The innovation lies in targeting neural circuits rather than cancer cells directly—a paradigm shift from traditional oncology. This approach involves developing Australia's first neural circuit-targeted cancer therapy platform, potentially transforming treatment for fatal childhood cancers.

Our progress

We have established significant preliminary findings across multiple research domains. Our spatial transcriptomics analysis revealed profound enrichment of synaptic signalling pathways in paediatric high-grade gliomas, with specific upregulation of both pre- and post-synaptic genes, demonstrating active bidirectional neural communication mechanisms. Using retrograde circuit tracing with patient-derived tumour xenografts, we mapped tumour-projecting neural circuits, identifying multiple brain regions that directly connect to tumour sites, including the pontine reticular nucleus, nucleus accumbens, and trapezoid body.
Our drug screening platform has evaluated over 2,200 compounds across patient-derived cultures, identifying 200+ promising candidates with anti-tumour activity. Importantly, we discovered that neural progenitor cells contribute to tumour growth, with marked increases in tumour size and proliferation when treated with neural progenitor cell-conditioned medium. These findings demonstrate how tumours exploit neural connection remodelling mechanisms, validating our hypothesis that targeting neural circuits rather than cancer cells represents a paradigm shift toward treatments.

What's next

With over one year remaining, we're moving full steam ahead to complete our neural circuit atlas. This fellowship enabled me to establish Australia's first neural circuit-targeted paediatric cancer research field, attracting a PhD student and securing additional UK Worldwide Cancer Research funding ($500K). We'll finalize circuit validation using DREADD technology and complete TRAP RNA sequencing. Our upcoming plans include validating potential anti-cancer drugs, increasing sample sizes, expanding drug screening, selecting drug targets and testing safety on healthy cells, and preparing manuscripts.

We welcome community support in disseminating research findings, recruiting students, and facilitating connections. Symposiums foster collaborations with international networks. We value guidance on regulatory pathways and connections with patient advocacy groups to accelerate discoveries into life-saving treatments.

THE KIDS' CANCER PROJECT

Dr Noa Lamm-Shalem

Children's Medical Research Institute

Funding provided via Project Research Grant

Targeting Nuclear F-actin to kill AKT-derived Paediatric Cancer

The project

We have identified that AKT activity in the nucleus is specifically oncogenic. While AKT has long been a therapeutic target, previous inhibitors were too toxic for clinical use. Our project focuses on selectively controlling Nuclear AKT to overcome therapy resistance and improve outcomes for children with sarcoma and AKT-driven cancers.

The problem

Children with cancer often respond to first-line therapy but then relapse because tumours evolve therapy resistance, a major barrier to cure across multiple childhood cancers. Relapse after standard treatment is frequently lethal and adding more chemotherapy or radiotherapy compounds lifelong toxicities. Although AKT is a validated driver of therapy resistance, pan-AKT inhibitors have shown unacceptable clinical toxicity, especially in children. Our project targets the specific, oncogenic activity of AKT in the nucleus and aims to selectively control Nuclear AKT, with the goal of restoring treatment sensitivity while reducing off-target effects, thereby improving survival and quality of life for young patients.

The why

For children with cancer, therapy resistance is a leading cause of treatment failure, often leaving few options for cure. Intensifying current treatments increases both immediate and lifelong side effects, which can significantly impact survivors' quality of life. Although AKT is a well-established driver of this resistance, past attempts to inhibit AKT broadly have failed due to high toxicity. By focusing on the nuclear AKT, which we have identified as specifically oncogenic, this project aims to develop highly targeted approaches that overcome resistance without minimal side effects; an essential step toward improving survival and life outcomes for young cancer patients.

Our approach

We focus on selectively targeting Nuclear AKT, identified as specifically oncogenic and a key driver of therapy resistance. Using osteosarcoma as our model and super-resolution microscopy, we uncovered the mechanism by which Nuclear AKT protects cancer cells from treatment and are developing strategies to disrupt this activity.

This novel, collaborative approach targets AKT by compartment, avoiding the broad inhibition and toxicity of previous pan-AKT inhibitors. By partnering with industry and engaging consumer advocates, it has high potential to restore treatment sensitivity and improve survival for young people with sarcoma and other AKT-driven cancers.

Our progress

Key discovery: We uncovered how Nuclear AKT drives therapy resistance in osteosarcoma. This critical finding lays the foundation for developing compartment-specific strategies to block this oncogenic activity.

Pipeline advancement: Early screens have already identified candidate approaches capable of selectively targeting Nuclear AKT while avoiding the broad inhibition and clinical toxicity of pan-AKT inhibitors. Collaborations: We have built strong partnerships with industry collaborators to accelerate lead optimisation and translation. In parallel, we have established active engagement with consumer advocates to ensure that research outcomes align with the priorities of young patients and their families.

Dissemination: Our findings have been presented at international scientific meetings and are now being incorporated into manuscripts, further amplifying the reach and impact of our work.

These achievements place the project in a strong position to move into the next phase of translating Nuclear AKT targeting into effective and safer therapies for children with cancer.

What's next

Mechanism to intervention: We will continue with hypothesis-driven research and drug screening to test strategies to disrupt this activity in osteosarcoma and other AKT-driven childhood cancers.

Lead optimisation: Advance the most promising Nuclear AKT–selective approaches, develop biomarkers to track activity, and validate candidates in robust preclinical models.

Collaboration opportunities: We seek partners in medicinal chemistry, structural biology, and paediatric oncology to help refine candidate compounds, access clinical samples, and shape trial-ready endpoints.

Support needed: Additional funding, access to resistant tumour models, and advanced imaging collaborations will accelerate translation.

Our goal is to nominate a Nuclear AKT–selective therapy ready for preclinical development, with the potential to restore treatment sensitivity and improve outcomes for children with AKT-driven cancers.

Dr Evangeline Jackson

University of Newcastle

Funding provided via Col Reynolds Research Fellowship

Targeting the metabolic dependencies of diffuse midline glioma

The project

Diffuse midline glioma (DMG) is the most lethal and rapidly progressing childhood cancer. Unfortunately, we currently lack brain-penetrant therapies that directly target the genetic drivers. As a result, an alternative treatment strategy is to target the major energy production pathways fuelling DMG growth, namely, the mitochondria and glycolysis.

The problem

DMGs are unique, driven by mutations in brain cells, particularly in the brainstem, that disrupt gene regulation, known as epigenetics. These tumours arise in regions where cells typically do not grow, or only during early brain development. As a result, although the underlying energy production pathways are not exclusive to DMG, they combine in unique ways to generate sufficient energy within these foreign microenvironments.

Research from around the world, including our own, has identified these distinct metabolic dependencies. My project aims to optimise novel brain-penetrant therapies to target the two major energy hubs, to improve outcomes for children with DMG.

The why

In Australia, brain cancer is the second most commonly diagnosed cancer in children, adolescents and young adults, representing around 15% of cancer diagnoses in children aged 0-14 years. DMG is diagnosed in approximately half of all children with high-grade glioma and patients face a devastating median overall survival of less than 9-15 months.

The treatment landscape for DMG patients is extremely limited, with the only approved treatment outside of clinical trials, palliative radiotherapy, not changing in over 60 years. Therefore, optimising new effective treatment strategies targeting the metabolic dependencies of DMG we hope will improve outcomes in combination with radiation.

Our approach

We have conducted sophisticated genetic depletion studies to identify the key drivers of DMG metabolism. This has enabled us to pinpoint therapeutic targets and understand how DMGs adapt to the loss of specific metabolic pathways, ultimately triggering a DMG-selective "metabolic catastrophe." Collaborating with industry partners, we have identified brain-penetrant therapies that target these metabolic vulnerabilities.

In our lab, we've established a high-throughput drug screening robot that is now helping us optimise dosing, timing, and treatment response, providing a refined regimen to test in living DMG models. We believe sequential treatments, rather than high-dose toxic combinations, will improve outcomes for patients.

Our progress

Proteomics analysis confirmed that both mitochondrial targeting drugs TR107 and ONC206 function similarly to dordaviprone, reducing the abundance of key mitochondrial proteins and inducing cell death. TR107 is ~100-fold more potent than dordaviprone in suppressing DMG cell growth. Our comprehensive review of PI3K/glycolysis inhibitors in high-grade gliomas, published in Neuro-Oncology, outlines both the limitations and potential of existing and emerging agents. Proteomics has identified that all four therapies under investigation; inhibit key PI3K pathway components at equivalent concentrations and induce robust cell death in DMG patient-derived cell lines. High-throughput drug screening combining mitochondrial ClpP agonists with glycolytic PI3K inhibitors, consistently reduces cell growth across five patient-derived cell lines. Several combinations, particularly those involving the novel brain-penetrant PI3Kα inhibitor GCT-007, demonstrated clear synergy.

Together, these findings validate mitochondrial and PI3K-glycolytic signalling as convergent vulnerabilities in DMG and establish a preclinical framework for rational combination therapy development.

What's next

Building on our comprehensive in vitro findings, our next priority is to translate the most effective drug combinations and sequence of therapies into relevant in vivo models. Our proteomic and functional screening data have highlighted consistent vulnerabilities across multiple DMG cell lines, particularly in mitochondrial and PI3K signalling. Several combinations, including those with TR107, ONC206, and the novel PI3Kα inhibitor GCT-007, have shown strong synergy in reducing DMG cell growth.

We now aim to test these combinations in living DMG models to define optimal dose, sequence, and timing, key factors for designing an effective, low-toxicity treatment regimen. We welcome collaboration on in vivo pharmacology, pharmacokinetics, and imaging to accelerate the translation of these therapies toward clinical application.

Dr Katherine Pillman

University of South Australia, Centre for Cancer Biology

Funding provided via Col Reynolds Research Fellowship

Improving the stratification of neuroblastoma patients to achieve better outcomes

The project

Using computational approaches on transcriptomic data, I am dissecting and deciphering inter- and intra-tumour heterogeneity in neuroblastoma. By mapping the landscape of differentiation stages, oncogenic drivers, and recurrent transcriptomic patterns, I seek to identify regulatory drivers of high-risk states and therapeutic vulnerabilities.

The problem

High-risk neuroblastoma remains one of the most difficult childhood cancers to treat, with high relapse rates and severe treatment toxicity. A major barrier is tumour heterogeneity, as little is known about which features of heterogeneous tumours drive disease severity, therapy resistance or recurrence. This molecular complexity is not captured by current clinical risk models, which poorly predict outcomes. The limited understanding of high-risk biology also hampers the discovery of new therapies.

To improve both treatment decision-making and therapeutic development, it is crucial to define the molecular underpinnings of aggressive disease and identify shared vulnerabilities as avenues for therapeutic targeting.

The why

For children with neuroblastoma, the consequences of misclassification are serious: some receive unnecessarily intensive treatment, while others relapse due to under-treatment. Current frontline therapies are intensive and toxic, capable of causing severe long-term side effects. Yet treatment decisions still rely on a limited set of clinical and molecular markers that fail to capture tumour complexity.

This lack of precision restricts our ability to deliver safer, more effective care. It also slows progress in therapeutic development, as we cannot identify shared vulnerabilities without first understanding the molecular features that define high-risk disease. A nuanced understanding is urgently needed to improve outcomes.

Our approach

My project is inherently collaborative, integrating bioinformatics (including gene regulatory network modelling and machine learning) with functional validation via CRISPR perturbation in stem cell differentiation models. This creates a powerful pipeline for identifying and validating disease drivers. This is an innovative approach to defining neuroblastoma heterogeneity at the single-cell level, using scRNA-seq to comprehensively characterise both transcriptomic profiles and genomic copy number variation - focusing on variation within as well as between tumours. Transcriptional features of aggressive disease will be identified using machine learning to integrate these molecular signatures (MYCN, mesenchymal programs, transcription factor regulons, CNVs) with clinical data.

Our progress

Used computational modelling of gene regulatory networks to identify candidate transcription factors that may drive high-risk neuroblastoma states; currently being validated by collaborators. Also uncovered candidate oncogenic microRNAs, with preliminary lab validation confirming their key role in development.

Curated, quality-controlled, and annotated single-cell transcriptomic and genomic data for ~120 neuroblastomas. CNV profiling is complete, and we are now scoring gene signatures for developmental stage and transcriptional states to define subtype composition and regulatory features.

Early results and expertise with our iPSC-derived model systems underpinned the recent success of a 5-year MRFF grant in childhood brain cancer, representing a further investment in the long-term success of my research program and childhood cancer collaborations.

Developed a collaboration with CCI researchers to perform drug screening on neuroblastoma PDX models, pitching a joint NHMRC Ideas application to combining molecular characterisation and drug response profiling to uncover therapeutic vulnerabilities and resistance mechanisms in high-risk neuroblastoma.

What's next

I'm excited to share ideas, find common ground, and build collaborations that bridge the gap between fundamental scientific discoveries and patient benefit, particularly in neuroblastoma. I'm especially keen to connect with clinicians, medical researchers, and data scientists working with neuroblastoma patients or clinical samples, to explore any opportunities to shape my work for the greatest and most immediate impact for children with cancer.

I would welcome discussion around the use of patient-derived organoids as models for neuroblastoma or medulloblastoma. From a career development perspective, I'd really value advice from senior computational biology group leaders, particularly on strategies for designing research for impact and building a strong, sustainable research program.

Dr Ryan Cross

Walter and Eliza Hall Institute of Medical Research

Funding provided via Col Reynolds Research Fellowship

Reprogramming Immune Cells to Fight Childhood Brain Cancer

The project

This project aims to develop new immune cell therapies to treat aggressive childhood brain cancers, including paediatric high-grade glioma (pHGG). By engineering immune cells to target newly discovered tumour markers, and combining synthetic safety switches and circuits, the therapy is designed to kill cancer cells while sparing healthy brain tissue.

The problem

The key challenge we're tackling is the lack of effective treatments for paediatric high-grade glioma (pHGG), one of the deadliest childhood brain cancers. It has proven resistant to current therapies, including chemotherapy, radiotherapy, and even many advanced targeted treatments. This is a critical issue for young people because it leaves them—and their families—with few options and devastating outcomes, highlighting an urgent need for innovative, life-saving therapies.

The why

This issue is critical for children, adolescents, and young adults because paediatric high-grade gliomas (pHGG) are among the most aggressive in this age group, often leading to poor outcomes despite intensive treatment. These tumours affect the brain, which controls essential functions like movement, speech, and memory—meaning that when many treatments are used, they can impact a young person's quality of life. The lack of effective therapies leaves families with limited options and immense emotional and physical burdens, making the development of safer, more effective treatments an urgent priority.

Our approach

Our approach uses cutting-edge immunotherapy by engineering a patient's own immune cells—CAR T cells—to recognize and destroy brain cancer cells. We've identified many new tumour-specific targets from real patient tumour samples, which we'll use to create a powerful set of CAR T cells designed specifically for paediatric brain cancers.

What makes this approach bold is the integration of synthetic biological circuits that act like "logic gates," helping CAR T cells distinguish between healthy brain tissue and cancer—significantly increasing safety, pushing the boundaries of what's possible in precision medicine for children with cancer.

Our progress

We've identified two novel synthetic safety switches and developed a new safety CAR, marking major advances in improving the precision and control of CAR T cell therapy for brain cancer. Our team has also begun incorporating AI and machine learning to prioritise and validate tumour-specific targets identified from real patient tumour samples, accelerating discovery and increasing translational potential. These achievements, alongside our expanding collaborations with leading clinicians, international academics, and experts in manufacturing, position us to rapidly advance safer and more effective CAR T therapies toward clinical application.

What's next

I am pursuing an ambitious research program aimed at accelerating CAR T cell and antibody therapy development by integrating large-scale synthetic construct libraries with AI-driven neural networks and reinforcement learning. This "lab-in-the-loop" framework is designed to rapidly iterate and optimise therapeutic candidates.

In parallel, I am investigating the application of large language models (LLMs) for synthetic de novo antibody design, with a focus on targeting antigens traditionally considered "undruggable." I actively seek collaboration and input from experts in AI-guided drug discovery, synthetic biology, high-throughput screening, and scalable genomic technologies to expand the frontiers of this work.

Dr Teresa Sadras

Olivia Newton John Cancer Research Institute

Funding provided via Col Reynolds Research Fellowship

Improving outcomes for relapsed acute lymphoblastic leukaemia

The project

This project investigates the biology of relapsed B-cell acute lymphoblastic leukaemia (B-ALL), a leading cause of cancer-related death in children. Focusing on sub-clonal heterogeneity and relapse post-immunotherapy, it aims to identify predictive biomarkers, uncover mechanisms driving treatment resistance and identify more effective, less toxic therapies for high-risk, relapsed childhood ALL.

The problem

Relapsed B-cell acute lymphoblastic leukaemia (B-ALL) remains one of the most difficult challenges in paediatric oncology. While frontline treatments cure most children, they are highly toxic and carry life-long side effects. Further, 10–15% of children relapse, with survival rates dropping sharply after each recurrence. Current therapeutic strategies are largely based on the disease at diagnosis, despite growing evidence that relapse is driven by distinct molecular changes and sub-clonal evolution. This project addresses the urgent need to understand the unique biology of relapsed B-ALL and develop more targeted, less toxic treatment strategies to improve outcomes for young people with cancer.

The why

While it is known that certain genetic features are associated with a higher risk of relapse, predicting which patients will relapse, especially among those with similar genetics at diagnosis has remained difficult. This limits our ability to tailor treatment and avoid over- or under-treatment. As newer therapies like immunotherapies are increasingly used, we also urgently need better laboratory models that reflect the complexity of relapse and treatment resistance. My work aims to develop and apply such models, enabling earlier identification of high-risk patients and better testing of novel therapies. This will support more tailored, effective, and less harmful treatment strategies.

Our approach

My research integrates innovative laboratory models and computational tools to investigate relapse in B-cell acute lymphoblastic leukaemia. I've developed novel, patient-informed models that replicate the clonal heterogeneity and treatment response seen in children with leukaemia, enabling the study of relapse across conventional and emerging therapies such as CAR T cells. In collaboration with bioinformaticians at Peter Mac, we've also established a new single-cell sequencing pipeline to track leukaemic cells in patient samples at diagnosis, during treatment, and at relapse. These approaches are revealing how leukaemic cells persist despite therapy and helping to identify early markers that may predict relapse risk.

Our progress

My achievements so far include strong collaborations with clinicians (Royal Children's Hospital), and Bioinformaticians (Peter MacCallum Cancer Centre), with three publications in preparation. This includes the report of our novel single-cell sequencing pipeline, which may be useful for other researchers. Earlier this year I was appointed as Head of the Leukaemia Biology and Functional Genomics laboratory at the Olivia Newton John Cancer Research Institute and named Deputy Co-Lead of the Haematology Research and Education Stream within the Victorian Comprehensive Cancer Centre Alliance. I'm also an invited member of the Children's Cancer CoLab researcher–clinician committee where I will contribute to identifying research gaps and organising events that bring together paediatric cancer researchers from around Victoria. I've presented my Fellowship work at leading international and national meetings, including the 2024 EMBO Workshop Intercepting Childhood Blood Cancer in Düsseldorf, at multiple seminars including the Cancer Flagship at the Murdoch Children's Cancer Institute.

What's next

Over the next year, I aim to publish three key manuscripts focused on relapse biology, predictive markers, and therapy resistance in B-ALL. I am continuing to work closely with clinicians at the Royal Children's Hospital and the Children's Cancer Centre Biobank to integrate clinical and genomic data. Looking ahead, I hope to expand our analyses to a larger cohort of paediatric ALL samples and would welcome collaboration with other national tissue banks and clinical teams to strengthen and validate our findings.

I also welcome input from consumers with lived experience of ALL to help ensure our research priorities remain clinically relevant and patient focused.

Prof Joost Lesterhuis

The Kids Research Institute Australia

Funding provided via Project Research Grant

Age is a critical driver of the paediatric tumour microenvironment and the response to immunotherapy

The project

We established a world-first fully 'paediatric mouse oncology clinic' and found that tumours grow much faster in paediatric mice compared to adult mice, with a vastly different immune response. Our results demonstrate that animal studies need to take young age into account for identifying new treatments in paediatric cancer.

The problem

Paediatric cancers originate in rapidly growing tissues within the context of a developing host. Yet, preclinical cancer studies invariably involve adult mice, even in paediatric cancer research. This practice may overlook crucial developmental influences on paediatric cancer cell biology, particularly when identifying and testing treatments that target the tumour immune microenvironment rather than cancer cell-intrinsic vulnerabilities.

This adult-biased preclinical approach could be an important reason why many new treatments in adults do not translate to young people with cancer.

The why

Cancer immunotherapy agents that have shown remarkable success in adults, such as immune checkpoint blockers, have shown disappointing results in childhood cancers. However, it is not known what causes this lack of responsiveness in young people with cancer, which makes it very difficult to identify new treatments that could render childhood cancers susceptible to immunotherapy.

Our approach

We identified age specific, host derived mechanisms underlying the anti-cancer immune responses in cancer mouse models of paediatric age. We comprehensively characterised the tumour immune microenvironment and response to immunotherapy using paediatric mice, in comparison with the same cancer models in adult mice.

Furthermore, we validated our results using clinical data from young people and adults. Importantly, we identified treatments that sensitised paediatric tumours to (adult) standard of care immunotherapies, resulting in increased cure rates in paediatric cancers. These findings underscore the significant influence of young age on cancer immune responses and reveal potential new therapeutic opportunities for paediatric cancers.

Our progress

We published the results in a preprint – www.biorxiv.org/content/10.1101/2025.07.16.663652v1 (currently under review, and second manuscript in preparation). We established paediatric models for leukaemia (ALL/AML), medulloblastoma, sarcoma and neuroblastoma and are actively collaborating with researchers across Australia and internationally, who want to use these paediatric mouse models. All data will be made publicly available upon publication of the manuscript.

What's next

Having now established that paediatric mouse models better reflect childhood cancer than adult models, we will investigate in detail how the immune response following current childhood cancer immunotherapy agents such as bi-specific antibodies in leukaemia and sarcoma, can be further improved to increase efficacy while not increasing toxicity.

In addition, we will investigate how the immune response in paediatric brain tumors can be leveraged for therapeutic benefit, in the context of current standard of care treatments such as radiotherapy.

Mr Bryce Thomas

University of Newcastle

Funding provided via Col Reynolds PhD Top-Up Scholarship

Modulating the Matrix to Mobilise Immunity: Therapeutic Potential of P-J4 in Paediatric High-Grade Glioma

The project

We have identified a new cancer-associated protein overexpressed in highly lethal paediatric brain tumours such as diffuse midline glioma (DMG) and medulloblastoma. This protein, termed Protein J-4 (P-J4) may negatively influence the tumour immune microenvironment (TIME) through modulation of the extracellular matrix (ECM) and is a potential new therapeutic target.

The problem

The extracellular matrix (ECM) is a fibrous network that surrounds the tumour and serves as a physical barrier while regulating several critical biological processes. It helps maintain tissue integrity by forming both physical and biochemical boundaries, and also facilitates cellular migration, proliferation, and blood vessel formation.

The ECM also plays a critical role in regulating communication between glioma cells and immune cells, through immune cell trafficking and inflammatory signalling and physical connections. Dysregulation of these processes causes a more immunosuppressive environment, suppressing the body's natural defence systems and creates a hostile environment, stopping potential therapies from targeting the tumour cells.

The why

DMG accounts for 50% of all paediatric high-grade gliomas (HGGs) and is responsible for 20–25% of all childhood cancer-related deaths. Median overall survival (OS) remains less than one year, with palliative radiotherapy currently the only standard-of-care treatment.

Promising therapies often reach clinical trials, but ultimately fail, largely due to an incomplete understanding of tumour-glioma biology, particularly the role of the extracellular matrix (ECM) and the immune system of these devastating tumours. Through this work, we aim to uncover new therapeutic targets and improve existing treatments giving children a better chance of long-term survival.

Our approach

DMG surface target interacting with their environment, were identified by an optimised native membrane enrichment technique followed by high-resolution quantitative proteomics. Using large-scale patient datasets and available RNA expression, genomics, and survival data, provided through collaborations with the Children's Brain Tumour Network and University College London, we explored the potential significance of P-J4 expression in paediatric brain cancer. Collaborations between the Murdoch Children's Research Institute and the Hunter Cancer Biobank provided 43 patient samples to confirm our findings histologically.

Finally, we have engaged Antibody Solutions to develop a humanised antibody that may serve as a future treatment target.

Our progress

Native membrane enrichment high-resolution proteomics identified high levels P-J4 in DMG, a protein typically involved in tissue development during embryogenesis and extracellular matrix, compared to normal control cells prepared analogously. These findings were supported by our bioinformatics analysis which correlated increased expression of P-J4 in low- and high-grade glioma cohorts with worse overall survival outcomes for patients overexpressing P-J4.

Ongoing work analysing 43 paediatric brain tumour samples will provide further information as to the location of the protein and its relationship to the TIME. Together this suggests a role for P-J4 promoting more aggressive glioma phenotypes, via modulation of the ECM and its impact on the local immune system.

We have also published a review article titled "Chimeric antigen receptor (CAR) T cells for Diffuse midline glioma" in Trends in Cancer, detailing the current landscape of CAR T therapies, and the significance of the TIME and ECM on therapeutic effectiveness.

What's next

Now that we have identified a identified a potentially new therapeutic target, we are excited to investigate the specific role it plays in modulating the ECM and its effect on the immune system. To achieve this, we are currently optimising our CRISPR-Cas9 knockdown models of P-J4 which will be used to perform functional validation studies to assess the impact on tumour cell growth, immune cell infiltration and signalling pathways, before progressing to mouse models to assess the impact on survival. Our ambition is to then use this information in conjunction with our new P-J4 antibody to develop a biologically relevant therapy to improve outcomes for children diagnosed with deadly brain tumours.

Mr Philipp Graber

Children's Cancer Institute

Funding provided via Col Reynolds PhD Top-Up Scholarship

Dissecting drug resistance and guiding targeted therapy in paediatric brain tumours

The project

We are developing 3D-printed models of childhood brain cancer using patient-derived samples to replicate the tumour environment and study how these cancers respond to drugs. Our aim is to determine whether these models can serve as alternatives to traditional systems, which often fail to reflect the complexity of tumours.

The problem

A major challenge in paediatric brain cancer research is the difficulty of growing tumour samples in the lab within a timeframe that is clinically useful. This is largely due to the absence of the tumour's natural environment and the long setup times required for animal models. By partially recreating this environment with 3D bioprinting, we aim to increase the number of patient samples that can be successfully studied.

The why

Many treatments that appear effective in early laboratory tests fail during clinical trials, often due to limited relevance of the models used and unacceptable side effects. This is especially concerning in children, who may face long-term consequences from those side effects. Our models aim to improve the preclinical testing, supporting the development of safer and more effective treatments.

Our approach

Using advanced bioprinting technologies, we can rapidly and accurately produce brain tumour models that can be adapted to the characteristics of individual tumours. We have also developed protocols to test a wide range of drugs, allowing seamless integration with precision medicine programs such as the ZERO Childhood Cancer Program.

Our progress

We have successfully developed and validated protocols for generating 3D bioprinted brain tumour models using patient-derived samples. These models demonstrate high cell viability and retain key genomic features of the original tumours. We have also optimised the system for high-throughput drug testing, enabling the screening of a broad panel of compounds. These achievements lay the foundation for integrating our models into precision medicine workflows and provide a platform for studying treatment response and tumour diversity.

What's next

We now plan to evaluate a larger set of patient samples and compare our models to those currently used in the ZERO Program. Our goals are to determine whether our models can complement existing ones and enable to grow more patient samples in a lab setting.

We also aim to investigate whether our models can better preserve biological diversity of the original tumours, which is important for understanding treatment resistance. It would be insightful to connect with researchers who have explored tumour diversity in different model systems to exchange insights and perspectives.

THE KIDS' CANCER PROJECT

Dr Donia Moujalled

Walter and Eliza Hall Institute of Medical Research

Funding provided via Project Research Grant

Inhibition of nicotinamide metabolism by the novel NAMPT inhibitor OT-82 potentiates venetoclax in paediatric and adult acute myeloid leukaemia models

The project

Our project aims to determine whether the altered dependence of relapsed/refractory AML leukaemic stem cells on nicotinamide metabolism can be therapeutically exploited to potentiate venetoclax using the clinical-stage NAMPT inhibitor OT-82. We demonstrate potent OT-82–venetoclax synergy in vitro, ex vivo, and in paediatric AML PDX models

The problem

Children diagnosed with acute myeloid leukaemia (AML) continue to face dismal outcomes, with survival rates stagnating for decades, in stark contrast to the success seen in paediatric acute lymphoblastic leukaemia (ALL). Standard treatments rely on intensive chemotherapy and stem cell transplantation, which carry significant toxicity and long-term complications. Venetoclax, a targeted therapy that revolutionised adult AML treatment, shows promise in children but is limited by the rapid emergence of resistance, especially in relapsed or refractory disease. Overcoming venetoclax resistance is critical to improve survival, reduce treatment toxicity, and provide young patients with durable, life-saving therapies where current options remain inadequate.

The why

Acute myeloid leukaemia (AML) in children, adolescents, and young adults remains a devastating diagnosis, with survival rates of less than 70% for newly diagnosed patients and far worse for those with relapsed or refractory disease. Standard chemotherapy is highly toxic, causing life-threatening complications and long-term side effects that significantly affect quality of life. Unlike in paediatric acute lymphoblastic leukaemia, progress has been minimal, and outcomes have not improved in decades. The emergence of resistance to new targeted therapies, like venetoclax, further limits treatment options. Addressing this urgent unmet need is critical to improve survival and provide safer, more effective therapies.

Our approach

Our research integrates cutting-edge laboratory and translational approaches to overcome venetoclax resistance in acute myeloid leukaemia (AML). We evaluate OT-82, a novel clinical-stage NAMPT inhibitor developed by our collaborators at Oncotartis (NY), in combination with venetoclax using in vitro AML cell lines, ex vivo patient samples, and in vivo patient-derived xenograft (PDX) models. This project is highly collaborative, engaging clinician-haematologists to access and profile paediatric/adult AML samples, ensuring direct clinical relevance. By combining innovative drug development, molecular profiling, and clinically informed preclinical models, our approach is both bold and translational, with the potential to significantly impact high-risk AML treatment.

Our progress

We have made significant progress in overcoming venetoclax resistance in AML through metabolic targeting with OT-82. In vitro, OT-82 demonstrated nanomolar IC50s against a diverse panel of AML cell lines and primary de novo and relapsed/refractory patient samples, inducing caspase-dependent apoptosis while sparing healthy CD34+ cells. Strong synergy was observed between OT-82 and venetoclax in venetoclax-resistant AML cell lines, mirrored by similar effects with another NAMPT inhibitor, KPT9274. In vivo, OT-82 potentiated venetoclax and venetoclax/azacytidine in venetoclax-resistant paediatric AML xenograft and PDX models, significantly extending survival compared to single agents.

Notably, paediatric PDXs (n=5) were highly sensitive to OT-82, with enhanced responses in combination therapy. We have now established Single Mouse Trials (SMT) in both paediatric and adult AML PDXs and optimised a targeted next-generation sequencing panel (~52 genes) to enable molecular profiling and identify biomarkers of OT-82 response, providing a strong foundation for biomarker-driven therapeutic development.

What's next

Our next steps focus on comprehensive molecular profiling to identify genomic and transcriptomic biomarkers that predict response or resistance to OT-82 and venetoclax in acute myeloid leukaemia (AML). Building on our ongoing Single Mouse Trials in paediatric and adult PDX models, we will integrate sequencing, transcriptomic analyses, and metabolomic assessments to uncover mechanisms driving treatment sensitivity. Correlating biomarker signatures with therapeutic outcomes will guide future patient stratification strategies and inform the rational design of biomarker-driven clinical trials.

By leveraging our existing collaborations with clinician haematologists and Oncotartis in New York, we aim to translate preclinical findings into actionable insights that enable precision treatment approaches for children, adolescents, and young adults with high-risk AML.

A/Prof Fernando Guimaraes

University of Queensland

Funding provided via Project Research Grant

Training natural killer cells for immunotherapy for children, adolescents and adults with sarcoma

The project

We're developing a new type of immune cell therapy to treat aggressive bone and soft tissue sarcomas in children, adolescents and young adults. By enhancing the body's natural killer cells, we aim to safely and effectively target tumours that don't respond to current treatments, moving closer to future clinical trials.

The problem

Young people diagnosed with aggressive sarcomas, such as osteosarcoma, Ewing sarcoma, and rhabdomyosarcoma, face limited treatment options and poor survival rates, especially when the cancer returns or spreads. For the past three decades, survival outcomes have barely improved, and current therapies often cause lifelong side effects.

This highlights an urgent need for safer, more effective treatments. Our project addresses this critical gap by developing a new form of immunotherapy that uses the body's own immune system to fight cancer, with the goal of improving survival and quality of life for young people facing these devastating diseases.

The why

Sarcomas often strike children, adolescents, and young adults at a time when they are growing, studying, and building their futures. Current treatments, surgery, chemotherapy, and radiation, are harsh and frequently lead to long-term physical and emotional side effects. Worse, if the cancer comes back or spreads, survival chances drop dramatically.

Despite decades of research, there have been no major advances in treatment or survival rates. This makes it critical to find new, targeted therapies that are not only more effective but also less toxic, giving young people the best chance at a healthy and fulfilling life after cancer.

Our approach

We are developing a new immunotherapy that harnesses natural killer (NK) cells, powerful immune cells naturally equipped to fight cancer. Using cutting-edge mRNA technology, we "train" these cells to better recognise and destroy sarcoma cells.

Our approach is bold yet safe, avoiding permanent genetic changes. It's built on strong collaboration between scientists, clinicians, and manufacturing experts, and aims to deliver an off-the-shelf therapy suitable for both children and adults. By combining innovative science with a clear path to clinical translation, we're tackling a high-risk, high-reward challenge with the potential to transform outcomes for young people with sarcoma.

Our progress

We recently published a landmark study in the prestigious Clinical & Translational Medicine journal demonstrating that mRNA-engineered natural killer cells can safely and effectively target paediatric sarcomas [https://pubmed.ncbi.nlm.nih.gov/39763064/]. This breakthrough gained significant media traction, reaching over 1.3 million readers across eight outlets, including Medical Xpress and New Zealand Doctor, with an advertising value equivalent of $12,928. Our team has established robust preclinical tumour models, clinical collaborations, and GMP manufacturing protocols.

Our former PhD student Dr Cui Tu, who completed her thesis on this project, is now a postdoctoral fellow and was recently awarded an Australia and New Zealand Sarcoma Association $40,000 grant to continue this work. Together, these outcomes underscore the novelty, momentum, and translational promise of our research in delivering new treatments for children and young adults with hard-to-treat sarcomas.

What's next

We are continuing to develop clinical-grade manufacturing protocols for our NK cell therapy at the Translational Research Institute (TRI) in Brisbane, building capacity for future clinical trials. In parallel, we are advancing health economic modelling with Prof. Haitham Tuffaha, using early cost-effectiveness data to inform strategic planning. We've secured preliminary data and co-funding partners to support large-scale grant applications, including a recent MRFF National Critical Infrastructure submission (outcome pending).

To progress toward first-in-human trials, we welcome new collaborators, funders, and community stakeholders to join us in shaping this innovative therapy's clinical translation and delivery for children and young adults with sarcoma.

THE KIDS' CANCER PROJECT

A/Prof Raelene Endersby

The Kids Research Institute Australia

Funding provided via Project Research Grant

DNA Damage Response Inhibitors Enhance the Efficacy of Radiation in Preclinical Models of Medulloblastoma

The project

This project investigates DNA-damage response (DDR) inhibitors as adjuvant therapies to enhance craniospinal irradiation (CSI) in medulloblastoma. Using orthotopic mouse models, DDR inhibitors significantly improved survival outcomes, especially with combined dosing strategies, offering promising avenues to improve front-line treatment efficacy and long-term cure rates in childhood brain cancer.

The problem

Medulloblastoma is the most common malignant brain tumour in children, yet survival rates have stagnated at around 70%, and relapse is almost always fatal. This highlights a critical need to improve front-line therapies to increase cure rates. Current treatments like craniospinal irradiation (CSI) are effective but limited by toxicity and resistance. Our project addresses this unmet need by enhancing CSI with DNA-damage response (DDR) inhibitors, aiming to make initial treatment more effective and reduce relapse. This is vital for young patients, offering the potential for longer, healthier lives with fewer long-term side effects.

The why

Children and adolescents with medulloblastoma face unique challenges. While initial treatments can be effective, relapse is almost always fatal, and current therapies often cause long-term side effects that impact development, cognition, and quality of life. Improving front-line therapy is critical not only to increase survival but also to reduce the burden of treatment. Enhancing craniospinal irradiation (CSI) with DDR inhibitors offers a way to make therapy more effective and potentially less toxic if they enable a reduction in CSI dose. Addressing this issue is essential to give young patients the best chance at long, healthy lives after cancer.

Our approach

We employed a high-throughput drug screen to identify drugs that could enhance front-line medulloblastoma therapies. This revealed DNA-damage response (DDR) inhibitors as especially effective drugs for MYC-driven medulloblastoma in combination with CSI. Using orthotopic mouse models and fractionated radiotherapy protocols, we tested multiple DDR inhibitors, targeting CHK1, ATR and WEE1, across different dosing strategies. Our approach is bold in its rigorous and thorough preclinical optimisations and assessments undertaken. It's novel in combining DDR inhibition with CSI, and collaborative across disciplines including oncology, radiation physics, and imaging. This strategy carries risk but offers high-impact potential to transform outcomes for patients.

Our progress

Our project has successfully identified DNA-damage response (DDR) inhibitors—prexasertib, ceralasertib, and adavosertib—as promising adjuvants to craniospinal irradiation (CSI) in medulloblastoma. Mechanistically, immunoblotting, flow cytometry and live cell imaging has revealed that these inhibitors function by dysregulating cell cycle checkpoints leading to increased radiation-induced apoptosis. Using orthotopic mouse models and clinically relevant fractionated CSI protocols, we demonstrated that DDR inhibitors significantly enhance treatment efficacy, with up to 75% tumour-free survival at 200 days. Bioluminescence imaging and immunohistochemistry confirmed reduced tumour burden and increased apoptosis. These findings represent a major step forward in improving front-line therapy.

We've established strong interdisciplinary collaborations across oncology, pharmacology, and imaging, and are preparing manuscripts for publication. Our work lays the foundation for future translational studies and clinical trial design. We have engaged with industry partners and international clinical trials consortia, including CONNECT, ITCC and LifeArc, to translate these findings and investigate potential applications in other paediatric cancers.

What's next

Combining DDR inhibitors with radiation may exacerbate long-term side effects, including cognitive deficits, especially in children. Our next steps involve assessing these risks using a unique research pipeline we have established to examine neurological impacts of novel cancer treatments in preclinical models. Most studies use adult mice, but our prior clinical and preclinical work shows children's brains respond differently.

We've pioneered use of paediatric mouse models and gold-standard neuropsychiatric testing to better reflect risks faced by young patients. We welcome advice from patient advocates to balance treatment effectiveness with long-term quality of life in early-phase trials. Support from experts in genomics, radiobiology, and drug development will be key to advancing safer, more effective therapies for children with brain cancer.

A/Prof Emmy Fleuren

Children's Cancer Institute

Funding provided via Project Research Grant

Deciphering the phosphoproteomic landscape of paediatric and AYA sarcoma

The project

Most young sarcoma patients do not harbour genetic mutations that current personalised therapies can target. We explored the utility of phosphoproteomics, an innovative technique that looks at protein activity, to identify potential drug targets that are not detected through standard genetic testing.

The problem

Sarcoma is an aggressive type of cancer that disproportionally affects children, teenagers and adolescents. Treatments have not changed dramatically in over four decades: no targeted therapies routinely exist, and standard-of-care (surgery/chemotherapy/radiotherapy) is accompanied with many side effects. Osteosarcoma, which grows in the bone, is particularly challenging: it is not uncommon to have already spread (metastasised) at diagnosis, and even surgery of a localised tumour often means amputation.

This underscores the unmet need to do better. We need to deliver strategies that are not only more effective, but also much less toxic, from diagnosis to the most advanced disease stages.

The why

One major barrier in improving outcomes for young sarcoma patients, is that most personalised cancer therapies are based on changes found in a tumour's genetic material (DNA). Most sarcoma patients do unfortunately not harbour such actionable genetic changes.

However, not all cancer-driving events happen in the tumour's DNA. Some occur directly in proteins, which are missed with standard genetic tests. An innovative technique called phosphoproteomics can detect changes in protein activity, and we have early evidence that some sarcomas do contain actionable protein changes. By identifying these, we may discover new treatment opportunities for patients who would otherwise miss out.

Our approach

This project, strategically embedded in the clinical ZERO Childhood Cancer program, is the first to study phosphoproteomic profiles of sarcoma across different disease stages, including early and advanced osteosarcoma. We hypothesised that in some cases, tumour growth is driven by abnormally activated proteins, making these attractive targets for therapy.

For selected candidates, we tested whether drugs that inhibit ("switch off") these proteins could stop tumour growth in patient-derived osteosarcoma cells grown in a dish in our lab ('in vitro') and in mini human osteosarcomas grown in mice avatars ('in vivo'), to build the most robust data to guide clinical decision-making.

Our progress

We established a multidisciplinary team including cancer researchers, bioinformaticians, clinicians and patient advocates from Children's Cancer Institute, Monash University, the ZERO program and the Cooper Rice-Brading Foundation.

We identified numerous activated proteins across sarcomas at different disease stages. Ten promising targets with matched drugs were selected for further validation in osteosarcoma. Two compounds, each targeting a cancer signalling pathway with enriched pathway activity in osteosarcoma versus other sarcomas, consistently outperformed other drugs across all tested osteosarcoma models, irrespective of disease stage. A combination of these two drugs enhanced anti-tumour efficacy in in vitro and in vivo osteosarcoma models and was well tolerated.

Research findings were presented at >14 occasions for diverse audiences (scientists/clinicians/students/community/industry) including eight major (inter)national cancer and sarcoma conferences (e.g. AACR/CTOS/ANZSA). The project's promise and quality is further recognised through various distinctions, including an international PhD scholarship, two travel/training awards, and a national and international poster prize.

What's next

Current priorities include dissemination of results, paving the way to (potential) clinical translation, and expanding our phosphoproteomics program. Specifically, we have advanced drafts of an original research article, review article and PhD Thesis on this project.

We are also scheduled to present at the quarterly Translational Medicine Workshop, designed to bridge the preclinical-clinical gap. As we, through both this project and our earlier work, evidently showed the promise of phosphoproteomics as a target discovery platform for childhood sarcoma, we are expanding on this success. Phosphoproteomics investigations form an important part of my new, multilateral discovery platform as part of my recently awarded Col Reynolds Fellowship, aiming to drive transformative contributions for more young sarcoma patients.

A/Prof Emmy Fleuren

Children's Cancer Institute

Funding provided via Project Research Grant

Exploiting the DNA damage response in paediatric sarcoma

The project

Outcomes for children with sarcoma are dismal and standard-of-care has many side effects. Early evidence suggests DNA damage response (DDR) inhibitors might be effective for some patients. We aim to understand who would benefit from DDR-inhibitors, by unravelling the DDR landscape of sarcoma and investigate its link with DDR-inhibitor sensitivity.

The problem

Sarcomas are a complex and diverse group of aggressive tumours that disproportionally affect children, teenagers and adolescents and young adults (AYAs). Better and kinder treatments are urgently needed. Recent evidence suggests that some sarcoma patients may benefit from a new type of drug, that targets a weakness in the cancer cell's DNA, called the DNA damage response (DDR). DDR-based drug combinations look particularly promising.

With numerous types of DDR-inhibitors out there, multiple potential drug combinations, and >100 subtypes of sarcoma, the unresolved question is: which young sarcoma patient will respond best to which DDR-inhibitor or DDR-based combination therapy, and why?

The why

Answering this will be crucial to bringing these novel treatments to patients in the clinic. Our interim analysis of the ZERO Childhood Cancer program illustrates this. While a substantial fraction of childhood sarcoma patients harbours a defect in their cancer cell's DNA suggestive of vulnerability to DDR-inhibitors, there is too little supporting data to prove if DDR-inhibitors would actually work. Most of these patients do hence not receive such drugs.

Our work will help bridge this gap. We aim to generate the experimental data that makes these drugs a treatment reality for patients who are otherwise missing out.

Our approach

Through the ZERO program, we have the unique opportunity to systematically map molecular DDR defects in one of the largest and most comprehensive cohorts of childhood sarcoma in the world. Our ability to test DDR-based drug combinations in our unique primary patient models and integrate these results with the patient's molecular DDR defects, perfectly positions us to pinpoint the clinically most rational, biomarker-guided DDR-based drug combinations. Our project's embedding in the ZERO program means our results are rapidly translatable, and can have immediate, predictive biomarker-driven clinical applications for young sarcoma patients. This is globally unique for childhood sarcomas.

Our progress

We comprehensively mapped molecular DDR-aberrations in >150 paediatric sarcoma patients. This revealed DDR gene defects in >50% of patients, plus a group of ~50 patients that harbour other molecular characteristics reported to be associated with DDR-drug sensitivity. Our in vitro (i.e. cells grown in a dish in the lab) drug testing results exceeded expectations, with three DDR-targeting drugs being profoundly effective already on their own, including cell kill in the best-responding sarcoma subtypes. We subsequently also identified 3 DDR-based drug combinations with remarkable efficacy in vitro and are making encouraging progress into pinpointing which DDR-inhibitor will work best for which sarcoma patient.
Research findings were presented at >10 occasions for diverse audiences (scientists/clinicians/students/community/industry) including oral presentations at two top international (AACR-JCA and FORTRESS) and national (ZERO National Symposium) cancer conferences. The project's promise and quality is further recognised through a highly competitive international PhD scholarship and two top-up scholarships.

What's next

Our current focus is on more precisely elucidating the molecular mechanism of response to the different DDR-inhibitors, to ultimately discover the best and most specific biomarker that can help predict who is most likely to benefit, and why that is the case. Drug testing in patient-derived sarcoma tumours grown in mouse avatar models is also on the agenda, though this was delayed as communicated previously.

We will actively continue with dissemination of research findings. We completed a review article on this topic which will be submitted soon, are putting together a publication plan for the original research article and a PhD Thesis will be completed for this project.

Dr Michelle Tennant

Murdoch Children's Research Institute

Funding provided via Col Reynolds Research Fellowship

RAD-VR: Creating Immersive Virtual Reality Environments to prepare paediatric patients for radiation therapy

The project

To co-design a state-of-the-art, VR intervention to prepare children with cancer (3-18 years) and their families for radiation therapy through education, simulation and exposure techniques. RAD-VR will be implemented and evaluated as standard paediatric radiation oncology care, measuring efficacy (anxiety, health literacy) and impact in terms of reduced GA use.

The problem

Radiation therapy (RT) is a cancer treatment frequently used in paediatric oncology to shrink and destroy cancer cells, often alongside surgery and chemotherapy. Acute distress is common among children and their carers undergoing RT due to intimidating environments, separation from parents, and the need for immobilisation devices and stillness during treatment. Procedural distress affects treatment adherence and increases reliance on general anaesthesia (GA) to ensure safe administration and compliance. Currently, all children under 3 and half aged 3–8 require GA for their treatment, which costs around $30,000 per child. Concerns are growing about the neurodevelopmental impact of repeated GA exposure.

The why

Radiation Therapy (RT) remains a cornerstone of treatment for paediatric cancers, particularly CNS tumours. Current clinical practice is to provide parent-directed education regarding the logistics and risks of RT; however, children rarely benefit from this mode of procedural education. General Anaesthesia (GA) is often required to ensure compliance. GA is also associated with significant anticipatory anxiety, requires fasting, increases the risk of medical complications, and adds burden to patients and families. It is also associated with negative postoperative behaviour changes in children, a slower recovery, sleep and eating disturbances, unknown longer term neurodevelopmental impacts and further medical trauma.

Our approach

RAD-VR is an immersive virtual reality (VR) intervention that prepares children for radiation therapy (RT) through simulation and psychologist-led coaching. It allows children to virtually tour the hospital, observe another child's treatment, and experience RT in first-person view, helping them manage procedural distress. RAD-VR is safe, easy to use, and well received by patients, parents, and healthcare providers. It improves understanding of RT, reduces anxiety, enhances cooperation during sessions, and lowers the need for general anaesthesia. Parents report it helps children feel confident and unafraid, making RT less confronting and potentially avoiding GA altogether.

Our progress

RAD-VR program of research commenced on February 1, 2025. Progress to date reflects the initial research planning period.

1. Legal
   – Research Collaboration and Intellectual Property Agreements between MCRI (sponsor) and trial site (Peter MacCallum Cancer Centre), drafted and in review
   – Tender for VR developer to build RAD-VR experience, complete
   – Service Level Agreement with selected company (Catalyst VR), complete
2. Ethics & Governance Approvals
   – Protocol (Phase 2 trial), in draft
3. Consumer Participation
   - RAD-VR presented to the Carer's Network, complete
   - Recruiting for consumer advisory group (Phase 1 Co-design), in progress
4. Project Management
   - RAD-VR SharePoint, complete
5. Public Awareness
   - Invited panellist - HIC Health, Innovation and Community conference August 2025
6. Professional Development
   – Competitively selected for ANDHealth's 2025 ACTIVATE program, 6-month accelerator to support RAD-VR translation and scale-up strategy (Phase 3), in progress
   – *Disruptions: 6 weeks secondary parent leave 15/2/25 - 29/3/25

What's next

Phase 1 co-design - between September -December 2025 we will prototype RAD-VR with clinician and consumer advisors and our VR developers, ready for Phase 2 roll out at our institution within an implementation trial. I am keen to meet and talk with anyone else working in the digital health space. Also, anyone conducting implementation research. In parallel, I am planning for sustainability and seeking to produce a business case for RAD-VR to be implemented permanently as standard care. I would welcome any mentorship from a business lens to support this aspect of the project.

Dr Karin Plummer

Griffith University, School of Nursing and Midwifery

Funding provided via Col Reynolds Research Fellowship

The DECIDE study: Codesign and evaluation of a co-designed e-health pain management decision aid for parents of children undergoing Bone Marrow Transplant

The project

DECIDE is developing and evaluating an e-health decision aid to support parents in making informed decisions about their child's pain management with their clinicians during bone marrow transplant. Co-designed with families and clinicians, the tool aims to improve shared decision-making, reduce distress, and personalise pain care throughout the transplant process.

The problem

Children undergoing bone marrow transplant experience prolonged and severe pain, but parents often feel ill-equipped to make informed decisions about pain management. Despite best intentions, uncertainty and communication barriers can result in under-treated pain or decisional regret. Currently, no tailored tools exist to guide parents through these complex choices. DECIDE addresses this gap by providing structured, evidence-based, and timely support for shared pain management decision-making.

By improving parental confidence and clinician-family communication, the study seeks to reduce pain and decisional conflict and regret during one of the most intensive treatments in paediatric oncology.

The why

The DECIDE study is a crucial initiative that addresses an urgent need, identified by consumers, to improve pain management. This will be achieved by promoting collaboration between healthcare providers and parents, who will work together to make informed decisions regarding pain management. This approach ensures that decision- making is transparent, informed and personalised to meet the unique needs of each patient. Improved pain management during HSCT therapy has many benefits, including reducing patient distress, minimising the risk of medical traumatic stress, and optimising time to analgesia.

Our approach

DECIDE is a digitally delivered, co-designed decision aid that supports shared decision making about complex pain-related care. It combines trauma-informed communication, evidence summaries, and personalised prompts in a format parents can access when and where they need it. The study uses mixed-methods, co-design approach that includes reviews of the evidence, audit of current pain management practices and workshops to ensure content is relevant and usable. What makes DECIDE innovative is its integration of design thinking, digital delivery, and real-world clinical insight to support shared decision-making in one of the most complex aspects of paediatric cancer care.

Our progress

We have completed Phase One of the DECIDE study, including formation of a multidisciplinary Steering Group, a systematic review, and interviews with parents and clinicians to explore decisional needs and conflicts in managing children's pain during bone marrow transplant (BMT). To complement this, we are conducting a retrospective audit to map current pain management practices, including opioid and adjuvant use, referral patterns, and adverse events. Findings from the review, audit, and interviews have informed the development of a prototype digital decision aid, designed to support shared pain management decisions during BMT. The study has received ethical approval and endorsement from the Australian and New Zealand Children's Haematology and Oncology Group.

Outputs to date include a pain decision needs framework for the DECIDE protype, a clinical summary of pain management options, and co-design-derived content priorities. Preliminary findings have been presented at national pain and oncology conferences, with manuscripts currently in preparation.

What's next

We are now advancing the co-design phase of the DECIDE study, drawing on insights from families, clinicians, and evidence synthesis to build a digital prototype that supports shared decision-making around pain during transplant. Development of the prototype is underway, incorporating trauma-informed communication, structured prompts, and accessible evidence summaries. The next step is acceptability testing with families and clinical teams to assess usability and relevance in practice. Feedback from this phase will guide refinements before we move into the final stage: real-world evaluation of DECIDE in clinical settings.

We welcome collaboration on digital implementation, culturally responsive adaptation, and future multicentre trial planning.

Dr David Mizrahi

The Daffodil Centre, University of Sydney

Funding provided via Col Reynolds Research Fellowship

From the ward to the playground: An active approach to childhood cancer

The project

My program of research is investigating the role of physical activity in children impacted by cancer. We explore barriers and facilitators among families and health professionals (via qualitative methodology), quantify physical muscle and cardiorespiratory deficits (via international collaboration) and deliver an online randomised trial of tailored exercise to survivors.

The problem

Physical activity is a key modifiable health behaviour for physical and psychological health. Young people impacted by cancer experience challenges in becoming physically active, which may increase their risk for future health complications. This is further complicated as many cancer services do not embed widespread physical activity support, so families lack appropriate guidance. My research program explores ways to promote physical activity to families and health professionals, to ensure young people are supported as they grow up with tools to improve their physical and psychological wellbeing and manage their health.

The why

Many children live with physical and psychological health consequences from their lifesaving treatment. This can leave them behind their peers as they grow up, which can further stigmatise them psychosocially. Survivors generally have low physical activity as a result, and thus as they grow up, they may be at even greater risk for cardiometabolic risk factors.

Innovations are needed in current models of care to support young people to find physical activities that are enjoyable and beneficial for them, so they can foster lifelong positive health behaviours, normalise their peer relationships and improve their health.

Our approach

Project 1: qualitative interview study of families and health professionals to explore how to support children who are undergoing active treatment, with the goal to innovate current models of care and explore implementation strategies.

Project 2: epidemiological study using St Jude (US) data to explore deficits in cardiorespiratory fitness, muscle mass and upper/lower muscle strength in young survivors and identify children at high-risk for deficits.

Project 3: A randomised clinical trial of online delivered tailored exercise delivered by exercise physiologists to children around Australia (MERRIER Study). The program is 5 sessions, consistent with Medicare's current model for implementation.

Our progress

Project 1: We conducted 28 interviews (17 health professionals, 11 consumers). Thematic analysis identified key barriers: 1. Lack of funded hospital-based programs and dedicated exercise staff, 2. Treatment-related side-effects, 3. Variability in referral patterns, 4. Need for flexible, patient-centred approaches. Four key facilitators were identified: 1. endorsement for being active during different treatment phases, 2. Parents' desire for structured, individualized exercise guidance, 3, Innovative strategies to promote engagement (e.g., utilising technology) and providing simple equipment (e.g. resistance bands, bike pedals). Manuscript being drafted.

Project 2: 478 participants from St Jude (US). Analysis ongoing, manuscript being drafted. Exercise intolerance was present in 55.2%, reduced lower body strength in 39.3%, reduced upper body strength in 28.2%, and 5.7% reduced lean muscle mass.

Project 3: The MERRIER Study is recruiting families from Camp Quality. To date, 22 children aged 5-18 have been enrolled (9 randomised to intervention, 6 control).

What's next

Project 1: After this publication, we open opportunities for new analyses of St Jude data. I am also co-leading (with Dr Lauren Ha) a Global Consortium study of 10+ already agreed sites internationally to explore fitness deficits and cardiovascular risk factors in young survivors.

Project 2: Our exploration using the RE-AIM framework will explore implementation factors for implementing a physical activity program/service during active treatment. We will be submitting grants to pilot its implementation, and welcome advice and collaboration in different settings.

Project 3: We have partnered with world-leading Wearables Hub (Sydney Uni) to analyse and interpret our activity tracker data. We will explore implementation factors for Camp Quality to deliver personalised exercise programs in the future.

Ms Rachel Edwards

Queensland Children's Hospital

Funding provided via Col Reynolds Research Fellowship

Optimising symptom management in paediatric oncology patients: Symptom PROMPT

The project

This study evaluates the use of patient-reported outcome measures (PROMs) and nurse-led interventions to improve symptom assessment and management for children undergoing bone marrow transplantation. It aims to enhance nurse knowledge, integrate systematic screening into care, and improve quality of life and treatment outcomes for paediatric cancer patients.

The problem

Children undergoing bone marrow transplantation (BMT) for cancer experience severe and often under-recognised symptoms that impact their quality of life. Despite evidence supporting symptom screening using patient-reported outcome measures (PROMs), these tools are rarely used in routine paediatric oncology care. Nurses—key to symptom management—often lack resources, skills, knowledge and confidence to act on symptom data, particularly psychological symptoms. This project addresses the critical gap in systematic symptom assessment and management. By equipping nurses with training and validated tools, the study aims to improve timely symptom recognition and response, ultimately reducing distress and enhancing outcomes for young people with cancer.

The why

Children, adolescents, and young adults undergoing cancer treatment, particularly bone marrow transplantation, face intense and complex symptoms that can significantly affect their physical and emotional wellbeing. When symptoms are not systematically assessed or addressed—especially psychological distress—they can lead to unnecessary suffering, reduced treatment adherence, and long-term health impacts. Current care does not routinely include patient-reported outcome measures (PROMs), leaving the young persons' voice unheard, symptoms potentially unrecognised, and not managed. Addressing this gap is critical to improving symptom control, enhancing communication between patients and clinicians, and ensuring holistic, patient-centred care that supports recovery and long-term quality of life.

Our approach

This mixed-methods study uses a novel, collaborative approach by co-developing interventions with key stakeholders, including clinicians and families, to ensure relevance and feasibility. It combines quantitative symptom data from validated PROMs with qualitative insights from interviews and focus groups to explore real-world implementation in a specialist paediatric BMT setting. A pre-post design evaluates changes in nurse knowledge, attitudes, and behaviours following tailored training. It integrates routine symptom screening into clinical care—an underused but evidence-backed strategy—aiming to transform how symptoms are identified and managed, improving quality of life and setting a foundation for national scale-up.

Our progress

Since the project's launch in October 2024, key milestones have been achieved. Governance processes have been completed, including the QUT funding agreement, deed of variation, and the CHQ contract and ethics. Strong collaborations have been established with the BMT clinical team at Queensland Children's Hospital and the ANZCHOG Nurses Research Group. A systematic literature review was completed, alongside parent and patient interviews and review of medical records. Patient recruitment continues. The online module, developed in the pilot study has been completed by 81 staff since October 2024. Three in-person skills development workshops were delivered, attended by 26 staff. Preliminary findings from the pilot study were presented at the Maddie Riewoldt's Vision Symposium and a project update was delivered to the ANZCHOG TACTIC group. Additionally, the project lead has served as a Research Ambassador for The Kids' Cancer Project (TKCP) at K'Day, strengthening engagement and advocacy for research in paediatric oncology.

What's next

In the coming months, key stakeholder focus groups will be conducted to explore barriers and enablers to implementing symptom screening into routine care. We will also be exploring IT solutions for integrating PROMs into clinical systems, and welcome advice or collaboration from teams experienced in digital health integration. Interviews with BMT nursing staff will be commenced to understand their perceptions of symptom management; we invite interest from other national sites to contribute to this work. Thematic analysis of all interview transcripts will follow, informing the development of practical, scalable implementation strategies.

We welcome support and shared learning from the broader paediatric oncology and digital health communities to strengthen the impact and sustainability of this research.

THE KIDS' CANCER PROJECT

Dr Christine Signorelli

University of New South Wales // Sydney Children's Hospital

Funding provided via Project Research Grant

The 'Engage' program: An equitable model of comprehensive cancer survivorship care for young cancer survivors

The project

'Engage' is an evidence-based, survivorship care program for young cancer survivors. It has been built to help survivors navigate survivorship care for the well-documented physical and psychosocial impacts of cancer and build survivors' self-management skills, through personalised, practical support that empowers survivors and improves long-term outcomes.

The problem

Engage addresses a key challenge that young survivors face in finding age-appropriate care that meets their significant and diverse unmet physical, psychological, and social needs, especially after treatment ends. These survivors face lifelong health risks, emotional distress, and difficulties in navigating complex healthcare systems. Our sustainable program ensures survivors receive appropriate, timely survivorship assessment, care planning, and intervention tailored to each survivor's unique constellation of developmental needs and chronic conditions. Addressing these gaps with tailored survivorship care is critical to empower young survivors to manage their health confidently and improve their long-term wellbeing.

The why

Children and adolescents/young adults (AYAs) with cancer have complex physical and psychosocial needs that often intensify when treatment ends. Despite being expected to resume education, work, and social life, many struggle with the lasting impacts of their diagnosis, which can affect long-term health, wellbeing, and life opportunities.

Successful transition back to "normal" life is critical to future functioning in survivorship, yet current systems often lack the time, resources, and tailored approaches needed to prepare them adequately. Without dedicated, age-appropriate survivorship care, this priority population risks poorer health outcomes and diminished quality of life well into adulthood.

Our approach

The 'Engage' program is an innovative, distance-delivered survivorship model—built on years of collaboration with young cancer survivors, clinicians, and community partners. It combines comprehensive health assessment, nurse consultations, multidisciplinary case review, and a personalised survivorship care plan with tailored recommendations for survivors and their GPs. This approach ensures equitable access, particularly for those facing health or geographic disadvantage, and directly strengthens survivor–GP relationships. Engage shifts survivorship care from hospital-centric to patient-centred, empowering survivors to self-manage complex, lifelong health needs. Its collaborative design and real-world feasibility position it to transform survivorship care and reduce long-term inequities in health outcomes.

Our progress

Over several years, our team has demonstrated the clinical effectiveness of Engage through a pilot (n=27) and large-scale evaluations in NSW hospitals involving >220 survivors and >30 stakeholders. We established its feasibility, safety, acceptability, and positive impact on survivors' quality of life and care experiences, particularly for rural and mobile young Australians. Process mapping and evaluation have produced an adaptable Implementation Framework and targeted tools for embedding Engage into care pathways.

This work, underpinned by strong clinical, research, and community partnerships, provides the expertise, infrastructure, and evidence base to co adapt the program for AYAs – the next step in our program of work.

What's next

Our next step is to adapt and expand Engage for adolescent and young adult (AYA) cancer survivors, co-designing the program with survivors, clinicians, and community partners to ensure it addresses their unique medical, psychosocial, and practical needs after treatment. We will refine and test the new AYA model in diverse settings, including rural and underserved communities, and evaluate its clinical effectiveness, cost-effectiveness, and scalability.

We welcome advice on sustainability strategies and health system integration, collaboration from clinicians, community organisations, and survivor advocates to strengthen engagement and reach, and support for technology solutions, training resources, and policy translation to embed survivorship care nationally.

Ms Chelsea Valentin

Sydney Children's Hospital Network

Funding provided via Col Reynolds PhD Top-Up Scholarship

The Role of Occupational Therapy in Paediatric Oncology

The project

Medical advancements have resulted in increased survival rates for children affected by cancer. However, little research has focused on children's development and their participation in life during and after treatment. With the potential to improve outcomes, it is essential to understand the role of occupational therapy in this vulnerable population.

The problem

The impact of cancer on a child's physical health and psychosocial wellbeing is well documented, lessening a child's ability to engage in normal developmental activities, form relationships, achieve academically, and maintain long-term wellbeing into adulthood.

However, there is an unmet need in literature focusing on a child's developmental and participation outcomes both during and after cancer treatment. With its core role to enable meaningful engagement in everyday life, this research examines occupational therapy (OT) in childhood cancer and will ultimately inform clinical practice by developing clinical guidelines that include OT as an integral component of holistic acute childhood cancer care.

The why

Childhood cancer impacts the ability to participate in daily routines (e.g. self-cares, play/leisure, school/productivity and rest). Emerging research has illustrated the crucial role OT has in paediatric oncology, through its unique role to promote health and wellbeing by enabling children to participate in activities they need/want to do.

Evidence suggests that OT should be an integral component of paediatric cancer care to optimise daily function and participation. However, the paucity of evidence addressing OT for children affected by cancer, particularly in early childhood (0-5 years), means no standardised clinical guidelines exist to ensure OTs continuously provide quality evidence-based care.

Our approach

My research program aims to i) understand health professionals' perspectives on current OT practices in paediatric oncology; and to ii) understand the developmental needs and experiences of children and their families throughout cancer treatment. Bridging both the clinical and research landscapes, this multi-perspective project draws on clinicians, academics and patients/families to build evidence-based OT practice in paediatric oncology, beginning with a systematic review on the impact of cancer on childhood development and how OT can mitigate these effects. Collectively, these data will ultimately inform standardised clinical guidelines to maximise a child's developmental outcomes and participation in everyday life.

Our progress

Key achievements include the completion of a systematic review, investigating the impact of childhood cancer on development, as well as the role of OT in mitigating these effects. 364 articles were identified as eligible for the review, with early results suggesting less than 20 papers globally examining OT interventions in the context of childhood cancer.

To support my work, I have been successful in obtaining two PhD top up scholarships, from Maridulu Budyari Gumal and The Kids' Cancer Project. I am committed to disseminating the findings of my work and raising awareness of the potential for OT in paediatric oncology, including my Randwick Emerging Researcher's Symposium poster and recent presentation at the Sydney Children's Hospital Network Grand Rounds.

The development of both a scientific advisory committee and a consumer advisory committee is underway to ensure the voices of these crucial stakeholders will inform this research project and its outcomes.

What's next

My research will next evaluate current clinical OT practices across Australia and New Zealand, then navigate how OT can best support the lived experiences of patients and families affected by childhood cancer. These findings will ultimately contribute to establishing evidence-based clinical guidelines. This has the potential to significantly transform the healthcare system and clinical practice to provide best-quality outcomes for all children affected by cancer.

Relevant clinician-researchers in the field of allied health and paediatric oncology are welcome to collaborate on this research. In addition, families of a child with cancer or childhood cancer survivors who are eager to support my research are greatly welcome to share their experience. This collaboration will shape my ongoing research plan and protocol.

Ms Jacqueline Hunter

University of Melbourne // University of New South Wales

Funding provided via Col Reynolds PhD Top-Up Scholarship

Exploring the Psychosocial Impact of Genomic Testing and Surveillance for Cancer Predisposition in Children

The project

This is an exploratory, psychosocial study. We aim to better understand families' experiences of germline genomic testing for genetic cancer predisposition in children with cancer, as well as families' experiences of routine cancer surveillance for children with a cancer predisposition syndrome.

The problem

Germline genomic testing is now available to all children diagnosed with cancer in Australia, exposing families to complex choices, information, and uncertainty. Little is known about how this testing affects families emotionally, psychologically, and practically. For families whose child is found to have a cancer predisposition syndrome, the added burden of ongoing cancer surveillance, often invasive and burdensome, is also underexplored.

Our project addresses this critical gap by investigating families' experiences to inform how genomic testing and cancer surveillance for genetic cancer predisposition in children are delivered, focusing on minimising distress and maximising satisfaction and clinical outcomes.

The why

Evidence shows that genomic testing and surveillance for genetic cancer predisposition can be distressing, burdensome, and anxiety-inducing for families - especially when children, adolescents, or young adults are involved. This age group is already navigating significant developmental, emotional, and psychosocial challenges, and the added uncertainty of genetic cancer predisposition can further disrupt their wellbeing and family dynamics.

To ensure that these complex processes are delivered in ways that minimise distress and negative impacts, it is critical to incorporate the perspectives of those directly affected into models of care. Doing so will improve patient and family experiences and enhance clinical outcomes.

THE KIDS' CANCER PROJECT

Our approach

This project utilises a multi-perspective, longitudinal, mixed-methods design to capture the complex experiences associated with genetic cancer predisposition in children. First, we conducted a systematic review to synthesise current evidence on families' perspectives and experiences with genetic or genomic testing and identify gaps in evidence.

Building on this, we collected in-depth data via questionnaires and interviews collected as part of psychosocial components embedded within larger clinical studies, across multiple participant groups (parents, patients, and clinicians) at multiple sites. Our novel approach integrates diverse perspectives over time and is embedded in clinical research, ensuring real-world relevance and supporting translation into practice.

Our progress

This study has so far resulted in two publications; a systematic review published in Genetics in Medicine (doi: 10.1016/j.gim.2024.101197) and an original article exploring healthcare professionals' experiences of an Australian germline genomic testing study, the PREDICT study, published in Cancer Medicine (doi: 10.1002/cam4.70680).

We have also completed our psychosocial study of families' experiences of the PREDICT study, which included 128 families (187 parents and 19 patients), with a manuscript currently under submission at British Journal of Cancer. We have recruited 13 families with a child with a cancer predisposition syndrome to our surveillance study, SMOC Junior, and data collection remains ongoing. Through SMOC junior, we have developed a partnership with the Sydney Children's Hospital Genetic Cancer Risk Clinic and are working with them to implement new clinical processes and develop future grant applications. We have disseminated project findings at five conferences and received $22,450 in additional funding or awards.

What's next

In the next phase of this project, we will continue recruitment and data collection for the SMOC Junior Study. Pending an ethics amendment, we plan to begin interviews with patients aged 12 and over participating in SMOC Junior to gain deeper insights into their experiences with surveillance. We are actively disseminating our findings at national and international conferences, including an upcoming poster presentation at the 2025 International Paediatric Oncology Congress (SIOP) in Amsterdam.

We welcome collaboration and input from the community in several areas, including feedback on our completed studies, opportunities to disseminate or build on our findings, and future collaborations that extend or apply our research in new contexts.

Ms Megumi Lim

Queensland University of Technology

Funding provided via Col Reynolds PhD Top-Up Scholarship

Financial Relief for Families affected by Childhood Cancer: A Discrete Choice Experiment

The project

Financial hardship is a significant challenge for families of children with cancer, often exacerbated by reduced income and increased expenditure.

This study aims to identify the preferences of parents and carers regarding financial aid programs for childhood cancer and explore heterogeneity in these preferences based on demographic factors.

The problem

For financial aid programs to be effective, it is important to understand the preferences of affected families and explore differences in these preferences across subgroups.

Identifying these preferences and their variation can guide policymakers and charities in prioritising and implementing proposed changes to financial aid models, ensuring they better meet the needs of affected families.

The why

Reliance on financial aid may be attributed to the higher out-of-pocket costs associated with childhood cancers, which are a consequence of the aggressive and unpredictable nature of the disease, and the demands of managing the medical sequelae of cancer survivorship. These factors hinder parents from maintaining or returning to employment.

Despite the availability of charities and financial support programs, many families report experiences such as near-homelessness, food insecurity, and prolonged financial recovery.

Our approach

The objectives of our study were to (1) quantify the relative importance of key factors influencing access to financial assistance and (2) examine whether parental or child health-related and demographic characteristics impact these preferences.

To achieve this, we employed a discrete choice experiment (DCE) study design, where participants made trade-offs between different attributes in hypothetical scenarios that mimic real-world decision-making. Based on the random utility maximisation model (RUM), this method assumes that individuals make rational choices and select the option that maximises their overall utility (satisfaction).

Our progress

The manuscript has been submitted to Supportive Care in Cancer and currently under review.

What's next

I would like some advice around how the study findings can be disseminated and implemented.

THE KIDS' CANCER PROJECT

Dr Lauren Ha

University of New South Wales

Funding provided via Project Research Grant

A digital health education program to improve childhood cancer survivors' self efficacy to engage in physical activity

The project

'Making Moves' (formerly known as iBounce) is a co-designed digital program that aims to engage childhood cancer survivors in physical activity. It includes online modules, exercise videos and tailored consultations with an Exercise Physiologist. My project aims to assess the effectiveness of Making Moves and concurrently explore its implementation potential.

The problem

My project addresses critical inequities in access to physical activity support for childhood cancer survivors, including those living in regional and remote Australia. Currently, there is no exercise service tailored to the unique needs of this population. This gap places survivors at greater risk of long-term health issues such as cardiovascular disease, obesity, and poor psychosocial outcomes.

My project responds to this unmet need by providing online physical activity education and individualised support. Additionally, my implementation trial will explore ways to support implementation of the intervention in the real world.

The why

Childhood cancer survivors may face long-term health problems, including cardiovascular disease and obesity. These late effects are worsened by physical inactivity and sedentary behaviours. Regular physical activity is safe and improves survivors' physical and psychosocial health, yet >85% are inactive and have poor fitness levels. For families living in regional/rural Australia, access to specialised care is limited and travel is financially taxing.

The lack of age-appropriate resources and exercise guidance for childhood cancer survivors presents a critical gap. Therefore, encouraging physical activity in survivors is essential, as poor lifestyle habits in childhood may continue into adulthood, compounding long-term health risks.

Our approach

My project is a Type I Hybrid Effectiveness-Implementation trial. To date, digital health physical activity interventions have shown to be feasible and acceptable among survivors and families. However, few studies have examined the factors that are crucial to their real-world implementation. The traditional process from intervention development to implementation is estimated to take an average of 17 years. My research is novel and bold, as hybrid study designs offer a potential solution to this delay by accelerating the process by examining both the effectiveness of the intervention and its implementation.

Our progress

We are close to completing long-term follow-up with all participants in the intervention. Our preliminary findings show survivors significantly increased their physical activity self-efficacy scores ($p<.01$), aerobic fitness levels ($p<.05$) and muscular strength ($p<.05$). A notable finding of our research was that the baseline fitness levels of participants (mean age 13 years) were equivalent to the fitness level of 60–69-year-old elderly population. This discovery is important as it spotlights survivors' less than optimal physical health and emphasises the need for health behaviour interventions that will improve health outcomes.

Regarding our implementation trial, we have completed all data collection and analysis and are currently preparing the manuscript for publication. We have further successfully published two articles and one letter to the editor in high impact journals from this project. We are also partnering with the charity, Little Big Steps, to expand Making Moves to support children newly diagnosed with cancer.

What's next

Upcoming plans for the project include finalising data collection and analysis for the Making Moves effectiveness trial. We are nearing completion of long-term follow-up with all participants and are excited to begin analysing the full dataset. In parallel, we remain on track to submit findings from our implementation trial for publication in a high-impact journal. These results will provide critical insights into both the effectiveness and real-world delivery of our intervention.

We welcome collaboration with researchers and clinicians interested in implementation science, digital health, health behaviours and childhood cancer care, as well as support in developing implementation strategies to tailor Making Moves across diverse settings.

THE KIDS' CANCER PROJECT

Dr Noemi Fuentes-Bolanos

University of New South Wales

Funding provided via Col Reynolds Research Fellowship

SMARCB1 and rhabdoid tumours: Building a transdisciplinary Research Framework

The project

Using a transdisciplinary approach that integrates epidemiology and multi-omics analysis, we aim to better understand a highly penetrant cancer predisposition syndrome in children affected by one of the most aggressive paediatric cancers (rhabdoid tumours).

This work may inform screening strategies and treatment decisions for a particularly vulnerable patient population.

The problem

Current reported data suggest that children with germline SMARCB1 mutations have a >90% likelihood of developing rhabdoid tumours. However, this estimate is based on reported cases and may be biased, as no formal epidemiological studies have been conducted in this cohort. This uncertainty complicates accurate counselling for families and may lead to overestimation of cancer risk. Additionally, rhabdoid tumours are highly aggressive and difficult to treat, making a deeper understanding of their biology essential.

Notably, it remains unclear whether germline SMARCB1 mutations influence tumour molecular signatures, potentially affecting tumour behaviour, treatment response, and overall prognosis.

The why

A diagnosis of rhabdoid tumour predisposition syndrome (RTPS) is devastating for families, with current data suggesting a >90% risk of cancer development within the first five years of life. Additionally, these tumours are highly aggressive and difficult to treat. Despite its severity, RTPS remains under-investigated. Intensive screening—currently recommended MRI every 3–4 months under general anaesthesia from birth—may benefit some patients, but it's unclear which subgroups truly require this frequency.

Focused research is urgently needed to refine risk estimates and optimise surveillance strategies for this vulnerable population.

Our approach

My research uses a transdisciplinary approach, combining epidemiological analysis, molecular oncology expertise, and national collaboration in clinical trial development to support families affected by rhabdoid tumour predisposition syndromes.

Currently, no established methodology exists to estimate penetrance in RTPS due to limited multi-omic and epidemiological data. Through the ZERO study, which enrols every newly diagnosed child with rhabdoid tumours, we aim to explore epidemiology in the Australian population alongside the Australian Cancer Registry. Collaborations with computational biology (Mark Pinese), international experts (Prof. Logan Spector), and molecular oncologists (Loretta Lau) supports the integrative approach.

Our progress

In the epidemiology stream of our research, we are analysing the incidence of rhabdoid tumours in Australia by age group using national data. We've initiated penetrance estimates by integrating genomic data with manual curation of gnomAD variants, providing the first refined risk estimates for SMARCB1 variant carriers—suggesting the true risk may be lower than previously thought. We've also completed molecular and RNA sequencing analyses of 30 cases enrolled in the ZERO study, comparing them with data from international cohorts and the Molecular Characterisation Initiative. These findings were presented at the 2025 ANZCHOG International Conference and the AACR Molecular Epidemiology Workshop. Additionally, the RTPS cohort has been included in a prospective clinical trial evaluating the utility of whole-body MRI (WB-MRI) for surveillance. This trial will also help assess the real-world cancer incidence in children with SMARCB1 mutations.

The first patient with RTPS has already been enrolled in the clinical trial.

What's next

Our next steps include completing the manual curation of general population variants, including CNVs, to finalise the epidemiology component of our study. We aim to integrate this with genomic data to refine penetrance estimates. Clinically, we are gathering more detailed patient information to correlate with current ZERO analyses and validate findings using international rhabdoid tumour cohorts. We also plan to engage families enrolled in SMOC Junior to understand their experiences and involve them in shaping future research directions.

We welcome collaboration in variant interpretation, data sharing, and family engagement strategies. Expanding SMOC Junior to include more families across Australia is a priority, and support from the community would be invaluable in achieving this.

Dr Joseph Yang

Murdoch Children's Research Institution

Funding provided via Col Reynolds Research Fellowship

Improving outcomes of childhood brain tumour surgery with advanced surgical image-guidance

The project

This project aims to develop an AI-powered tractography tool to improve surgical planning for children with brain tumours. Early benchmarking shows current tools are unreliable near tumours. We are building a curated paediatric imaging dataset and collaborating globally to create accurate, accessible, and safer tractography for paediatric neurosurgery.

The problem

This project addresses the critical need for safer surgical planning in children with brain tumours, a leading cause of childhood mortality in Australia. Surgery near vital brain fibre tracts carries high risk, especially in developing brain. Tractography, which maps these pathways using MRI, is essential but current tools are slow and outdated.

At the Royal Children's Hospital Melbourne, I have over a decade of experience applying advanced tractography in paediatric neurosurgery. Leveraging one of the largest clinical imaging datasets, we propose to develop an AI-powered, automated tractography tool tailored to children, enabling faster, safer, and more accessible surgical planning.

The why

Accurate and timely tractography is essential for guiding brain tumour surgery in children, where even minor surgical injury to critical white matter pathways can result in permanent functional impairment. These tracts control vital functions like movement, language, and vision, and damage can lead to lifelong disability. The consequences extend beyond the child, profoundly affecting their families and quality of life.

As survival rates improve, preserving neurological function becomes increasingly important. Quick, reliable tractography helps neurosurgeons avoid harm to these structures, ensuring safer surgeries and better long-term outcomes for paediatric brain tumour patients and their families navigating life after treatment.

Our approach

The approach combines expert-defined tractography with AI to create an automated solution tailored for paediatric brain tumour surgery. I have benchmarked existing tools, revealing critical failures near tumours, and are now building a curated dataset that accounts for tumour-altered anatomy.

This novel dataset underpins AI model training and international collaboration. By retraining existing algorithms and automating expert workflows, I aim to improve tractography speed, accuracy, and clinical utility. This work addresses a high-risk clinical gap and stands out through its deep integration of neurosurgical insight, real-world imaging data, and global research partnerships to deliver safer, AI-enhanced surgical planning tools.

Our progress

We benchmarked six leading automated tractography methods against expert-defined tracts in 14 children undergoing brain tumour surgery. While most performed well on the healthy side, accuracy declined significantly near tumours, with errors at tumour margins posing potential surgical risks in 76% of cases. These issues stemmed from inconsistent tract definitions and failure to account for tumour-induced anatomical changes, highlighting the limitations of current automated tools in paediatric neurosurgery. Findings were presented at OHBM and ISMRM 2025, with a manuscript underway.

Ongoing work includes building a curated RCH imaging dataset with manually segmented tumours to support AI training. We also re-trained TractSeg using 60 epilepsy cases, showing promising alignment with expert-defined language tracts. Further testing across diverse conditions is planned. In parallel, we are automating key steps in our expert pipeline, including noise-cleaning and ROI seeding, in collaboration with international research groups to improve accuracy and scalability of paediatric tractography tools.

What's next

Curating high-quality clinical imaging data is resource-intensive, with tumour variability adding complexity. We are prioritising the development of a well-structured internal RCH database to support future AI training, testing, and international collaboration. We will also evaluate existing automated tractography in varied clinical scenarios, starting with 35 patients with bottom-of-sulcus dysplasia as a model for small, cortically based tumours.

Strong international interest has been generated through early presentations and existing collaborations with leading groups in North America and Europe. Future plans include engaging UK paediatric neurosurgery centres. This fellowship has provided dedicated time to establish this foundational work, bridging clinical neurosurgery and advanced neuroimaging to enable safer, AI-driven tractography for children undergoing brain surgery.

THE KIDS' CANCER PROJECT

Dr Rachael Lawson

Children's Health Queensland

Funding provided via Col Reynolds Research Fellowship

IMplementation of genomic testing and software-informed dosing interventions to improve dosing of chemotherapy in children with cancer (IMPROVE)

The project

This project implements genomic testing and software-informed dosing to personalise chemotherapy in children with cancer. By integrating pharmacogenomic data and Bayesian forecasting tools, the study aims to improve drug safety, efficacy, and individualisation of busulfan dosing, setting a scalable model for broader precision medicine implementation

The problem

Current chemotherapy dosing for children with cancer typically uses standardised approaches that fail to account for individual variability in drug metabolism. This can result in suboptimal treatment, either underdosing, which increases the risk of cancer relapse, or overdosing, which raises the likelihood of severe, sometimes life-threatening toxicities.

Young patients are especially vulnerable to these effects due to their developing organs and unique physiology. Our project addresses this critical gap by implementing genomic testing and model-informed precision dosing, aiming to personalise therapy, reduce toxicity, and improve survival outcomes for children undergoing high-risk cancer treatments like stem cell transplantation.

The why

Children and young people with cancer are especially vulnerable to dosing inaccuracies due to developing organs and unique drug metabolism. They face fewer clinical trials, complex protocols, and dosing schedules that often ignore age-related changes (ontogeny).

Standard dosing increases the risk of relapse or serious toxicity, and young patients are more affected by long-term treatment side effects. While Bayesian forecasting software enables personalised dosing, it remains underused due to limited validation in clinical outcome studies and minimal training for clinicians. Addressing these challenges is essential to improve safety, efficacy, and long-term outcomes in paediatric cancer care.

Our approach

This project integrates pharmacogenomic testing and Bayesian forecasting software into clinical care to personalise chemotherapy dosing in children. We are prospectively evaluating the impact on drug exposure and clinical outcomes, supported by a multidisciplinary team of clinicians. The approach is bold, translating complex model-informed dosing into clinical practice. The fellowship is highly collaborative: internationally, I serve as Vice Chair of the BuGene01 Study, invited due to my research leadership. Nationally, I collaborate with experts including Prof. Rachel Conyers and Prof. Jason Roberts. Emerging partnerships with TKCP researchers further strengthen the project's translational potential.

Our progress

The project has achieved key early milestones, including ethics approval BuGene01, integration of pharmacogenomic testing into clinical workflows, and implementation of Bayesian dosing software (DoseMeRx) for busulfan at QCH. Education modules for clinicians have been developed and piloted at QCH and will be made available to other centres by the end of 2025. Data has been collected for 149 patients with full sampling post each busulfan dose and outcome data. This will be used to review multiple population PK models in Bayesian forecasting software and outcome analysis. BuGene SSA and contracts are underway with the hope to open at the first site in Q4 of 2025. Collaborative partnerships have been strengthened nationally and internationally, including active leadership in the BuGene01 study. A manuscript on model-informed dosing was accepted for publication January 2025, two other manuscripts are under preparation, and early findings and progress have been presented at national forums.

What's next

We will open to patient recruitment, recruit to BuGene01 study and be involved in the analysis and manuscript. Evaluate clinician feedback on the education package. The next phase will expand model-informed dosing to other high-risk drugs (e.g. fludarabine, voriconazole), with development of implementation tools to support broader clinical use. A national symposium is planned to share findings and facilitate uptake across paediatric oncology centres- ANZCHOG26.

I welcome advice from the TKCP community on implementation science and real-world outcome analysis. Support with clinician training frameworks and digital integration would strengthen our impact. We are also seeking collaborations with other centres interested in piloting precision dosing approaches or contributing data for multicentre validation to ensure robust and scalable outcomes.

Dr Marion Mateos

Children's Cancer Institute

Funding provided via Col Reynolds Research Fellowship

Providing hope for children with high-risk brain cancer

The project

My project focuses on two key challenges in paediatric brain cancer – developing more effective therapy for children with diffuse midline glioma (an incurable cancer) using information from the normal health cells ("germline"); as well as developing a more sensitive method to detect brain cancer in spinal fluid ("liquid biopsy").

The problem

Brain cancer is the leading cause of disease-related death in children. Both aims of my project could facilitate new treatment and disease monitoring approaches in childhood brain cancer.

Recent research shows that brain cancer caused by malfunctioning DNA repair genes in the normal healthy cells ("germline") may respond to novel therapy including immunotherapy; however, germline-directed treatments have been limited so far in brain cancer. Furthermore, standard monitoring, including brain scans and spinal fluid examination, may miss early disease recurrence ("relapse") in brain cancer. This indicates that more sensitive monitoring approaches are needed to detect relapse early and maximise disease control.

The why

New approaches to treating brain cancer in children are urgently required to address the dismal outcomes facing the children we treat. My research will uncover the role that the germline plays in a specific type of incurable brain cancer called diffuse midline glioma, through collaboration to establish the largest ever international cohort to answer this question.

Detection of early relapse, through development of more sensitive liquid biopsy monitoring will allow treating oncologists to understand when the treatment is working; or when there are signs of early relapse that require a different, more effective treatment approach to prolong survival.

THE KIDS' CANCER PROJECT

Our approach

Germline: I established an international collaboration spanning the UK, Germany, US, Canada and Australia, which profiled 252 children diagnosed with diffuse midline glioma. Using matched tumour and germline DNA sequencing data, along with RNA sequencing, we have addressed for the first time how prevalent germline mutations are in diffuse midline glioma. Liquid biopsy: I established a workflow with colleagues at Children's Cancer Institute to collect spinal fluid and isolate circulating tumour cells from children with brain cancer. Samples at subsequent time points will allow us to assess changes over time in the tumour cells from these patients.

Our progress

My first-author publication in Neuro-oncology highlighted that 7.5% of children (19/252) diagnosed with diffuse midline glioma had a germline mutation, which was identified as a cancer-causing gene in adults but not previously shown to be important in diffuse midline glioma. The germline mutation led to cancer development in 1% of cases (2/200 patients), which is novel.

In a world-first, we have detected circulating tumour cells (CTCs) in the spinal fluid in children with brain cancer. We have performed single cell RNA sequencing on cells from 18 patients and demonstrated that these matched the primary brain tumour. Detection of these CTCs was more sensitive in some cases than standard cytology. These data will allow us to monitor changes over time that may indicate how cancers evade current treatments.

Two MRFF-funded national partnerships (>$17 million AUD, under embargo), an international partnership (Cambridge) and Neuro-oncology podcast have emerged from this work.

What's next

Next steps in the germline work include: 1) understanding patterns of drug sensitivity in diffuse midline glioma cells, that relate to key DNA damage repair pathways uncovered by my recent published work; 2) establish a larger international dataset with RNA sequencing; 3) plans to establish a biobank. This has been accelerated due to concurrent work with TKCP Col Reynolds Fellow (Dr Fuentes-Bolanos) and a recently awarded Brain Cancer MRFF grant ($3 million, under embargo) to develop models of germline mutations.

The liquid biopsy work will be leveraged to look at changes in cancer cells over time, during treatment. We will also collaborate with Cambridge to evaluate the immune cell populations that are present in children with brain cancer.

Prof Richard D'Andrea

University of South Australia

Funding provided via Project Research Grant

Integrating cancer germline genetics, precision medicine and oncology to optimise clinical management of childhood AML.

The project

We are working with the ZERO Childhood Cancer program to integrate germline findings into clinical management. Our over-arching aim is to improve outcomes for childhood acute myeloid leukaemia (AML), preventing missed diagnoses of cancer predisposition, reducing risks for haematopoietic stem cell transplant and improving access to genetic counselling and surveillance.

The problem

Approximately 50 children are diagnosed annually in Australia with AML, 40% of whom will relapse with dismal prognosis. Germline variants in cancer predisposition genes (CPG) are critical for prognostication, treatment and outcomes. The ZERO platform is facilitating integration of germline findings from genomic analyses into treatment and genetic counselling; however, this is associated with several challenges. Our collaborative, multidisciplinary team is addressing these with the aim of improving treatment and quality of life and reducing the trauma for families that face the burden of understanding familial cancer risk in addition to substantial hospital stays and costs required for treatment.

The why

Identification and reporting of important germline variants has several critical implications for treatment of childhood AML patients:

1. Avoiding a stem cell transplant from a related donor with a high-risk cancer predisposition which may result in a donor cell-derived leukaemia or be associated with poor donor cell function.
2. Providing information that can minimise treatment toxicity when patients harbour a germline variant affecting a biochemical pathway important for sensitivity to cytotoxic drugs.

3. Identification of undiagnosed cancer predisposition syndromes, allowing genetic counselling for families, genetic testing to identify gene mutation carriers, and consideration of surveillance for at-risk family members.

Our approach

We are leveraging the extensive resources, data and expertise of the ZERO childhood cancer framework. We aim to discover new classes of germline risk variants and establish new paradigms for incorporating germline genetics into treatment of childhood AML, so that critical cancer risk information derived from personalised genomics is included in life-saving treatment decisions, enabling individualised cancer treatment to improve outcomes for childhood AML. We are using a suite of bioinformatic approaches for discovery of new germline CPG variants. Our multidisciplinary team is also identifying and addressing the roadblocks for incorporating germline information into clinical management.

Our progress

1. We have identified high-confidence, potentially pathogenic germline structural variants (SVs) in 37 AML patients. Through integration of somatic mutations, other germline variants and gene expression alterations from ZERO's pipeline, we are now focusing on SVs with a clear loss-of-function mechanism.
2. We have established a clinical questionnaire for collection of patient response data for ZERO AML patients. This will be integrated with our findings from germline genomics analyses to identify germline variants that are implicated in the prolonged haematological recovery and severe toxicity following chemotherapy.
3. To develop clinical guidelines informed by a consensus building process and including approaches to diagnosis, curation and reporting of germline variants in childhood AML we have developed a survey to seek perspectives on a range of issues from a panel of experts. Through discussion and revision, we will develop consensus guidelines that will be a key resource for AML clinical management.

What's next

We will continue to work towards bridging the gap between the vast germline information now available from precision medicine programs such as ZERO, and the diagnosis of familial predisposition, which is critical in AML patients for clinical decisions such as treatment intensity and stem cell transplant. While ultimately this project aims to advance the methodologies and clinical utility of germline genomics for childhood AML, we appreciate input from other childhood cancer research groups and clinicians on the integration of germline information from sophisticated genomics platforms to improve detection, knowledge and reporting of CPG variants, and for development of guidelines informing treating clinicians of the considerations and risks for their patients and their families.

THE KIDS' CANCER PROJECT

Dr Hannah Walker

The Royal Children's Hospital

Funding provided via Col Reynolds PhD Top-up Scholarship

BREATH: Breathe Easier After Transplantation 'Haematopoietic', helping children to breathe easier after transplantation by understanding infectious and inflammatory complications

The project

This project has three key aims; to better precept which children are at risk of lung disease, improve how we diagnose these complications and therefore lead to more targeted treatments. One way we will do this is by multiomic immunological profiling of samples collected from children undergoing bone marrow transplant.

The problem

Haematopoietic stem cell transplantation (allo-HSCT) remains the only curative treatment option for many children with relapsed and high-risk leukemia. Whilst curative for the underlying condition, allo-HSCT can unfortunately result in pulmonary complications in up to 25% of patients, with mortality in up to 30% of those affected.

The mechanisms underlying the development and trajectory of specific pulmonary diseases post-HSCT are not well understood and as a result there are no strategies for early detection and limited therapies to target the underlying diseases process.

The why

Survival for children undergoing allogeneic HSCT has improved dramatically over several decades due to optimisation of supportive care. Unfortunately, pulmonary complications post-HSCT continue to be devastating for children and families, leading to intensive care unit admission and worse overall survival. At present we have few techniques to determine which patients are at higher risk of these complications occurring or ways to prevent the pulmonary disease from developing. Better methods for early detection of these pulmonary complications are therefore urgently required prior to the development of the most severe pulmonary disease, that is often irreversible and responds poorly to treatment.

Our approach

This innovative research project applies novel techniques, pioneered and optimised by the team at MCRI in children with cystic fibrosis, to post-HSCT patients at RCH. This involves longitudinal multio-omic immune profiling on airway fluid (and paired peripheral blood) collected via broncho-alveolar lavage in asymptomatic and symptomatic children pre and post HCT. The aim of this work is to which to identify immunological signatures associated with both lung disease post HCT but also lung health. These techniques have not been applied in combination to the HCT cohort before and sampling of asymptomatic children pre and post HCT is particularly novel.

Our progress

Awards

Picchi Award for Excellence in Cancer Research; Clinical Science Category 2025
Awarded top 10 publications in Clinical and Translational Immunology for 2024-2025 for paper ' Pulmonary complications post allogeneic transplant in children'; invited to present in person at Australian and New Zealand Society of Immunology Meeting Dec 2025; Best Abstract in the Junior Investigator category; clinical research at the Australian and New Zealand Children's Oncology (ANZCHOG) Conference 2023

Outputs

13 publications from 2024-2025; five as first author.
-1.) This includes the multi-institutional collaborations, involving designing a novel primary endpoint which utilised the data collected during my PhD thesis on the adaptive platform trial BANDICOOT, led by CI A/Prof Rachel Conyers, DOI https://doi.org/10.1016/j.jtct.2025.01.894.
2.) Output from the PhD project which involved a multi-site retrospective collaboration with Perth Children's Hospital which identified pulmonary complications occur commonly and contribute significantly to mortality post HCT doi: 10.1002/cti2.70003. eCollection 2024 Sep.

What's next

This project will act as a pilot study with the vision to expand to other transplant centres nationally and characterise lung disease in a larger validation cohort. The future aims will be to expand to a National and International biobank of biological samples and prospective data outcomes for these children.

Future translational studies, utilising these samples, will enhance the collaborative research generated by the Victorian Paediatric Cancer Consortium to understand and model the biological drivers of post-HSCT lung disease, identify disease modifying therapies to halt and reverse the insult to the lungs and ultimately enhance survivorship. Future involvement from consumers to design future studies will be welcomed and essential to the excess of the study expansion and future clinical translation.