The Kids' Cancer Project Symposium Abstracts

All abstracts listed below are in the Translate research pillar.

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TRANSLATE

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.

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.

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.

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.