Children's Cancer Institute

STUDENT PROJECTS 2025

Children's Cancer Institute

UNSW SYDNEY

CHILDREN'S CANCER INSTITUTE

A Message from the Executive Director,

Professor Michelle Haber, AM

Like every one of you, here at Children's Cancer Institute, we believe that a life should be long. That every child should have the chance to grow up, grow old, chase their dreams, and fulfil their potential.

Today, as a result of medical research, eight out of ten children will survive their cancer. But, unfortunately, nearly three children in Australia are still dying from this disease every week. We believe this is three too many.

From the very beginning, our focus has been to cure all children with cancer and eliminate their suffering. While we are getting closer to this aim, there is so much more to do.

Children's Cancer Institute is the only independent medical research institute in Australia wholly dedicated to putting an end to childhood cancer. We use a multi-pronged approach to tackling childhood cancer by investigating causes and prevention, improving diagnosis and monitoring and developing more effective treatments, with the overall goal of saving the lives of all children with cancer and improving their long-term health outcomes, through research.

Based at the Lowy Cancer Research Centre at UNSW, we have world-class facilities and global collaborations with researchers and clinicians. In 2025, we will be moving into the Minderoo Children's Comprehensive Cancer Centre (MCCCC), the first of its kind in Australia and a world-class facility to accelerate the implementation of discoveries into standard care for children with cancer. MCCCC is a collaboration between Children's Cancer Institute, the Kids Cancer Centre at Sydney Children's Hospital, Randwick, and UNSW Sydney, that will ultimately bring together over 900 clinicians and clinical staff, researchers and academics into a new integrated facility, all with the sole focus of curing children's cancer, delivering globally leading research, education and clinical care.

Children's Cancer Institute nurtures an environment of innovation, collaboration and learning. We are committed to fostering the next generation of research leaders. As one of our students, you will be provided with personalised training in state-of-the-art facilities and will be mentored by internationally renowned research leaders with a strong focus on training the future generations of cancer researchers.

Student opportunities at the Institute are listed in the following pages. If you are interested in exploring these further, please get in touch with the listed supervisor. If you are interested in a particular area of research but do not find a project that appeals to you listed here, we encourage you to contact the leaders of these programs directly to discuss a project to best suit both you and the research team.

By joining Children's Cancer Institute, you have the opportunity to work at the forefront of cancer research and really make a difference in the lives of children with cancer. I look forward to welcoming you to Children's Cancer Institute,

Michelle Haber

CHILDREN'S CANCER INSTITUTE

RESEARCH FACILITIES, PLATFORMS & TECHNOLOGIES

Children's Cancer Institute (CCI) was established in 1976 and is the only independent medical research institute in Australia wholly dedicated to curing childhood cancer. With over 350 staff and students, CCI is internationally recognised as a leading child cancer research institute.

CCI is known for its research excellence in neuroblastoma and other high-risk childhood cancers including leukemia, brain tumours and sarcoma, and has received widespread international recognition for its ZERO Childhood Cancer national child cancer precision medicine program (ZERO) which is currently being rolled out to every Australian child with cancer, irrespective of type or risk of their cancer, or where in Australia they live.

Click here to take a virtual tour of Children's Cancer Institute!

Facilities & Resources

- State-of-the-art PC2 laboratories
- Core Services team to facilitate the efficient day-to-day operation of the labs
- Own animal facility, where expert staff provide researchers with training and advice
- Close relationship with clinicians at the Kids Cancer Centre (KCC), Sydney Children's Hospital, providing access to many thousands of clinical tumors, blood, serum, bone marrow and other tissue samples for research use.
- Robust computing and technology capabilities to support its critical research efforts.
- CCI Cell Bank: quality managed, STR-validated, mycoplasma-free stocks of over 20 of the most widely used cancer cell lines
- CCI Tumour Bank: over 9000 paediatric cancer patient samples ranging from frozen or cryo-preserved tumour tissue to cryo-preserved extracted blood products derived from bone marrow and peripheral blood.
- The ZERO Childhood Cancer program, Australia's national personalised medicine program, available to every Australian child with cancer. Led by Children's Cancer Institute and the Kids Cancer Centre at Sydney Children's Hospital, Randwick, ZERO is a true multidisciplinary team effort of researchers and clinicians and includes all nine of Australia's children's hospitals together with 22 national and international research partners.
    - Conducting in-depth genomic analysis for each child enrolled, ZERO aims to improve survival, reduce side effects, and advance science's understanding of childhood cancer for the benefit of all.
    - With over 1400 patients enrolled on ZERO, researchers have unique access to thousands of biospecimens with linked clinical data from high-risk patients spanning the full range of childhood cancers.
    - Through ZERO, in addition to the biospecimens, we also have a unique database of linked molecular information including Whole Genome Sequencing (WGS) for both tumor and

germline, as well as tumor whole transcriptome sequencing (RNA seq) and methylome data on all of the patients enrolled in ZERO.

- The number of samples with linked clinical and molecular data will increase dramatically over the next 5 years.

Platforms and Technologies:

The ACRF Drug Discovery Centre

Established in 2010, the ACRF Drug Discovery Centre houses a sophisticated array of advanced automation equipment and technology to integrate biological assay data with chemical compound information. The facility also provides dedicated specialist scientists with expertise in high-throughput small molecule screening, providing support for drug discovery research. With an extensive library of 320,000 diverse novel compounds, over 6000 known bioactives and FDA-approved agents (including 114 FDA-approved oncology drugs), specialised cutting-edge instrumentation for high-throughput liquid handling, automated high-content screening, various other equipment such as plate readers, as well as advanced data management systems, the facility is primed to support researchers in their drug discovery journey. In 2020, the Drug Discovery Centre expanded to incorporate an exciting new drug discovery initiative called 'THerapeutic INnovations for Kids' (THINK). THINK is an end-to-end drug discovery and development capability dedicated to generating new therapies for rapid clinical application in children with cancer.

The ACRF Child Cancer Liquid Biopsy Facility

The ACRF Child Cancer Liquid Biopsy Facility is the first of its kind in Australia and provides infrastructure and expertise to enable the development of non-invasive disease monitoring techniques to inform risk-adjusted treatment regimens. The state-of-the-art facility houses a suite of complementary technologies for enrichment and purification of CTCs (FACS Fusion and microfluidics), precision dispensing of single cells (CellenONE) and platforms to conduct both single cell RNA Sequencing (BD Rhapsody) and single cell DNA Sequencing (MissionBio Tapestri). Additionally, it has been designed to provide access to ultrasensitive molecular pipelines dedicated to the analysis of low input and cell free DNA.

The ACRF Spatial Immune Oncology Facility

The Institute will also soon house the ACRF Spatial Immune Oncology Facility, containing the latest cellular and sub-cellular spatial multiomic profiling technologies. Combined with the ability to create bespoke tissue microarrays, access to high dimensional cytometry and advanced protein profiling tools, the facility will provide the equipment and expertise to accelerate the development of more effective immunotherapeutic approaches and stratification systems for children with cancer and to generate a complete view of the tissue immune microenvironment in paediatric cancer to date.

Bioinformatics Platform

CCI has a dedicated team that oversees all the bioinformatic data analysis for every research team at the Institute, as well as aiding clinicians at the Kids Cancer Centre in the Sydney Children's Hospital. This includes developing and maintaining next generation sequencing pipelines with the latest bioinformatic algorithms for analysis of whole-genome and exome sequencing, transcriptome sequencing, targeted sequencing, single-cell RNA sequencing, ChIPseq; as well as microarray analysis, drug sensitivity, biomarker discovery, and risk prediction analysis. CCI has recently transitioned from an in-house HPC to a cloud-based analysis platform, which is available to all researchers at CCI not just bioinformaticians and computational biologists.

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Minderoo Children's Comprehensive Cancer Centre

Minderoo Children's Comprehensive Cancer Centre (MCCCC) signals a new era of hope for kids with cancer. Australia's first dedicated children's comprehensive cancer centre, MCCCC promises to deliver tomorrow's care today — transforming experiences and outcomes for children and young people with cancer.

MCCCC builds on a strong history of collaboration. Children's Cancer Institute and the Kids Cancer Centre (Sydney Children's Hospitals Network) share an almost 40-year history of working together to translate laboratory discoveries into clinical trials and medical care. MCCCC maximises the potential of this collaboration by bringing together the Children's Cancer Institute, Kids Cancer Centre and University of New South Wales in a formal partnership with a shared strategy and co-located in a purpose-designed building. Together we will improve outcomes for children and young people with cancer, by transforming the cancer journey from diagnosis through treatment and into survivorship.

Due to open at the end of 2025, Australia's first children's comprehensive cancer centre, MCCCC will include:

- a 900-strong community of dedicated child cancer professionals: clinicians, scientists, and allied health workers
- state-of-the-art technologically advanced wet and dry laboratory spaces
- education, training and research spaces
- new oncology inpatient units designed with a child and family focus
- a new outpatient treatment centre with capacity to deliver a range of therapies now and into the future.

CHILDREN'S CANCER INSTITUTE

STUDENT SUPPORT

Our students bring great energy and enthusiasm, providing fresh ideas and perspectives to tackle the complex challenges faced in childhood cancer research today. As a student, you will be guided and mentored by a dynamic team of world class researchers who have strong collaborative links with research and clinical teams throughout the world. In addition to this, you will have access to a comprehensive professional development program run by a dedicated team focussed on career development, state-of-the-art equipment and facilities, professional support staff, access to a full range of laboratory services and opportunities for overseas travel to present at conferences and work with collaborators. You will also receive the support of your peers through the Children's Cancer Institute Student Association (CCIStA) that runs activities throughout the year, including an annual student retreat.

POSTGRADUATE TOP UP SCHOLARSHIP

We offer a Top Up Scholarship for up to 4 years to students who have been awarded a competitive scholarship, eg. a Research Training Program Scholarship or similar. The value of the scholarship is dependent on the base award of the individual's stipend. All students who have been awarded a competitive scholarship will be topped up to a total of $40,000 P/A.

CHILDREN'S CANCER INSTITUTE

JOSEE HILTON EXCELLENCE AWARD

These tax-free, competitive awards will be offered to a value of up to $10,000 AUD per annum and are offered to students demonstrating exceptionally high potential who have succeeded in attracting a primary competitive scholarship such as an APA. This Excellence Award is in addition to the top-up scholarship.

HONOURS SCHOLARSHIP

We offer two Honours year scholarships of $5,000 tax free annually. Selection is based on academic achievement throughout the undergraduate degree, interest in cancer research, personal qualities, as well as other evidence as may be deemed relevant to future success in the area of biomedical research. Scholarships are awarded for one year and are not deferrable.

Applications for Honours year scholarships will be open in July each year and close in early-November.

HOW TO BECOME A STUDENT

1. Browse the information and lists of student projects in this booklet.
2. Identify an area of interest, contact a potential supervisor and arrange a suitable project. When you contact potential supervisors, please include a CV and your most recent academic transcript.
3. Submit an admissions application to the University of New South Wales (UNSW). Honours students must be accepted into an Honours program in an appropriate UNSW Faculty. PhD students should successfully fulfil the requirements for admissions through UNSW.
4. Coordinate with your supervisor to obtain clearances from the appropriate Ethics Committees.
5. Begin your research program.

HONOURS

The standard duration of enrolment for an Honours degree is one academic year, actual dates for the Honours programs you may enrol in can vary, so please consult the websites below for more detailed information.

When you undertake an Honours project at Children's Cancer Institute you will be enrolled in a UNSW Honours program. Therefore, you need to meet the UNSW Honours entry criteria. For information regarding the Honours Programs at UNSW that students may be enrolled in, please visit the following websites:

- https://www.unsw.edu.au/science/student-life-resources/honours-how-apply
- https://www.unsw.edu.au/science/our-schools/babs/student-life-resources/student-resources/honours
- https://www.unsw.edu.au/medicine-health/our-schools/biomedical-sciences/student-life-resources/honours/soms-honours

POSTGRADUATE STUDIES (MASTERS/PhD)

The majority of PhD students at the Institute are enrolled through the Faculty of Medicine, School of Clinical Medicine, Paediatrics, Course Code 1825 Child Cancer Research. Dr Fa Valdes Mora is the Institute's Postgraduate Coordinator and is responsible for advising supervisors and Higher Degree Research (HDR) candidates on all academic and administrative matters relating to their candidature.

UNSW Graduate Research School

The UNSW Graduate Research School is the central administrative and support unit for all higher degree research students and their supervisors at UNSW. The website below will direct you to information on admissions requirements and enrolment procedures to undertake postgraduate study at UNSW together with links to scholarship application forms for both local and international students.

https://research.unsw.edu.au/graduate-research

RESEARCH GROUPS

Listed below are our Research Groups and their Leaders. Please take a look at our website for more information on their areas of research focus. We are always looking for enthusiastic students interested in our research.

BRAIN TUMOURS GROUP

Group Leader

Prof David Ziegler ✉ DZiegler@ccia.org.au

Senior Scientist
Dr Maria Tsoli

Senior Scientist
Dr Ben Rayner

CANCER EPIGENETIC BIOLOGY AND THERAPEUTICS GROUP

Team Leader and Theme Head (Therapeutic Discovery); Post-Graduate Coordinator for UNSW Centre for Childhood Cancer Research

Dr Fa Valdes Mora ✉ FValdesMora@ccia.org.au

CANCER TARGETS AND THERAPEUTICS GROUP

Research Fellow

Dr Angelica Merlot ✉ AMerlot@ccia.org.au

CHEMICAL BIOLOGY AND TARGET BASED THERAPIES GROUP

Team Leader

Dr Jean Bertoldo ✉ JBertoldo@ccia.org.au

COMPUTATIONAL BIOLOGY GROUP

Group Leader and Deputy Director (Enabling Platforms and Collaboration)

A/Prof Mark Cowley ✉ MCowley@ccia.org.au

COMPUTATIONAL DRUG DISCOVERY BIOLOGY GROUP

Group Leader

A/Prof Antoine de Weck ✉ ADeWeck@ccia.org.au

CHILDREN'S CANCER INSTITUTE

EMBRYONAL CANCER THERAPY AND PREVENTION GROUP

Group Leader

Prof Glenn Marshall GMarshall@ccia.org.au

Senior Scientist
A/Prof Belamy Cheung

EXPERIMENTAL THERAPEUTICS & MOLECULAR ONCOLOGY GROUP

Group Leader and Executive Director

Prof Michelle Haber MHaber@ccia.unsw.edu.au

Principal Scientist
A/ Prof. Jamie Fletcher

Group Leader

Prof Murray Norris MNorris@ccia.org.au

Senior Scientist
Dr Klaartje Somers

FUNCTIONAL GENOMICS OF LEUKAEMIA GROUP

Team Leader

Dr Charles de Bock CDeBock@ccia.org.au

GENE DYSREGULATION GROUP

Group Leader

A/Prof Tao Liu TLiu@ccia.org.au

GENE THERAPEUTICS AND DRUG DELIVERY GROUP

Team Leader

A/Prof Joshua McCarroll JMccarroll@ccia.org.au

GENOMIC CHILDHOOD CANCER RISK GROUP

Team Leader

Dr Mark Pinese MPinese@ccia.org.au

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LEUKAEMIA BIOLOGY GROUP

Group Leader and Theme Head (Cancer Biology)

Prof Richard Lock RLock@ccia.org.au

Senior Research Officer
Dr Patrick Connerty

Senior Research Officer
Dr Narges Bayat

METAL-TARGETED THERAPY AND IMMUNOLOGY GROUP

Team Leader

A/Prof Orazio Vittorio OVittorio@ccia.org.au

MOLECULAR DIAGNOSTICS GROUP

Principal Scientist

Dr Michelle Henderson MHenderson@ccia.org.au

SARCOMA BIOLOGY AND THERAPEUTICS GROUP

Team Leader

Dr Emmy Fleuren EFleuren@ccia.org.au

TRANSLATIONAL TUMOUR BIOLOGY GROUP

Group Leader and Deputy Director (Research Themes)

A/Prof Paul Ekert PEkert@ccia.org.au

Senior Scientist
Dr Emmy Dolman

TUMOUR BIOLOGY AND TARGETING GROUP

Group Leader

Prof Maria Kavallaris MKavallaris@ccia.org.au

RESEARCH PROJECTS

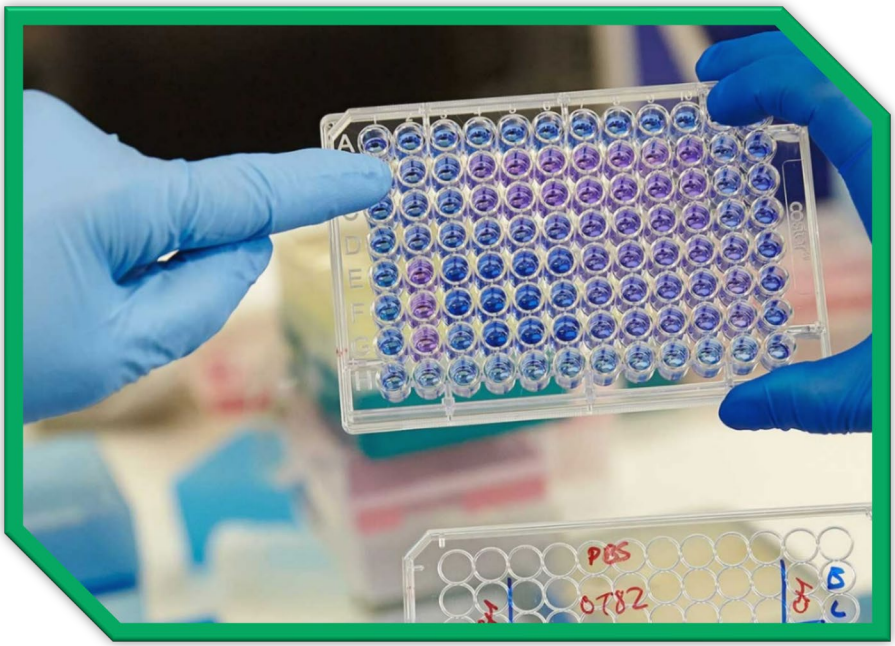
BRAIN TUMOURS GROUP STUDENT PROJECTS

Project Title: **Targeting drug resistance in paediatric high-grade glioma**
Supervisor: Prof David Ziegler DZiegler@ccia.org.au
Dr Rebecca Lehmann RLehmann@ccia.org.au
Suitable for: Honours Students
Project outline:

Paediatric high-grade glioma (pHGG) is a devastating form of brain cancer with an extremely poor prognosis. The BRAFV600E mutation has recently been discovered as a driver mutation in a subset of pHGGs, with tumours driven by this mutation responding to targeted BRAF and MEK inhibitors. Unfortunately, resistance inevitably develops, resulting in disease progression. Our laboratory has derived several drug-resistant BRAFV600E mutant pHGG cultures, which display resistance to the drugs commonly used in the clinic. This project will involve identifying potential therapeutic targets in these in vitro models of drug resistance, and subsequently determining the efficacy of novel therapies. A wide range of in vitro techniques will be used and if interested, students can use this project to develop skills in bioinformatics.

Project Title: **Developing targeted therapies for paediatric ependymoma**
Supervisor: Dr Maria Tsoli MTsoli@ccia.org.au; Dr Kenny Ip KIp@ccia.org.au;
Dr Joan Chen JChen@ccia.org.au
Suitable for: Honours Students
Project outline:

Paediatric ependymoma is a challenging brain cancer with limited treatment options. This project will focus on targeting key players identified through genomic analysis and enhancing them by identifying effective combinations using high-throughput screening (HTS). Additionally, novel targeted therapies will be identified through CRISPR to address key aberrations such as EZHIP and RELA fusions. The study will involve a combination of in vitro and transcriptomic techniques to uncover potential therapeutic targets and evaluate novel treatment strategies.



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Project Title: Developing novel treatment approaches in high-risk childhood medulloblastoma

Supervisor: Dr Aaminah Khan akhan@ccia.org.au
Dr Marion Mateos m.mateos@unsw.edu.au

Suitable for: Honours students

Project outline:

Brain cancer is the leading cause of disease-related death in children (1). Medulloblastoma is the most common malignant brain tumour of childhood (2). Children with medulloblastoma demonstrate varying survival rates based on the age of presentation, clinicopathological features, presence of MYC amplification and high-risk DNA-methylation grouping (3-6). While standard risk medulloblastoma has a cure rate of >80%, children diagnosed with high-risk medulloblastoma (e.g Group3, Group4 (7, 8)) have cure rates less than 50% (3). Furthermore, patients with high-risk medulloblastoma including those with MYC oncogene amplification or overexpression are not curable at disease relapse. There is, therefore, an unmet need to develop novel therapeutic approaches including novel drug combination therapies for children diagnosed with high-risk medulloblastoma.

Our lab is a prestigious brain cancer group with proven impact in preclinical development and translation of research to clinical trials for children with brain cancer.

In order to develop novel combination strategies, we will determine the most effective and compelling single agent drugs to take through to the next stage of our combination testing. Targeted inhibitors for key pathways known to be upregulated in medullblastoma, based on previous work from our group and others, will be evaluated. These include the homologous recombination repair pathway (e.g ATR inihibitor), the PI3K/mTOR pathway (eg novel brain penetrant inhibitor paxalisib) compared to conventional cytotoxics.

The successful student will develop key wet lab skills and work with brain cancer cells lines, in vitro drug treatments and drug efficacy readouts. Statistical analysis skills will also be developed. This work will lay the key foundation for further work in combination screening and synthetic lethality experiments, to improve treatment options for children with high-risk medulloblastoma.

CANCER TARGETS AND THERAPEUTICS STUDENT PROJECTS

Project Title: Specific Targeting of Tumour-Promoting Cancer-Associated Fibroblasts in Pancreatic Cancer

Supervisor: Dr Angelica Merlot AMerlot@ccia.org.au
Dr Dong-Hun Bae DBae@ccia.org.au

Suitable for: Honours, Masters or PhD Students

Project outline:

Importance of the project:

- Pancreatic cancer remains a death sentence with only 10.7% of patients living 5 years after diagnosis
- Cancer Associated Fibroblasts contribute to disease progression, chemoresistance and metastasis
- Cancer Associated Fibroblasts can be either *tumour promoting* or *tumour inhibiting*
- This project aims to develop novel therapeutics that target tumour promoting Cancer Associated Fibroblasts, while sparing tumour inhibiting Cancer Associated Fibroblasts to improve patient outcomes.

What the project will involve:

- This study will use cell culture (a range of cells lines, including patient derived pancreatic cancer cells), fresh patient tissue, molecular biology techniques, fluorescent/confocal microscopy, mouse models, patient samples, *etc*.
- Feel free to contact Dr. Angelica Merlot to have a chat about whether the project matches your interests.

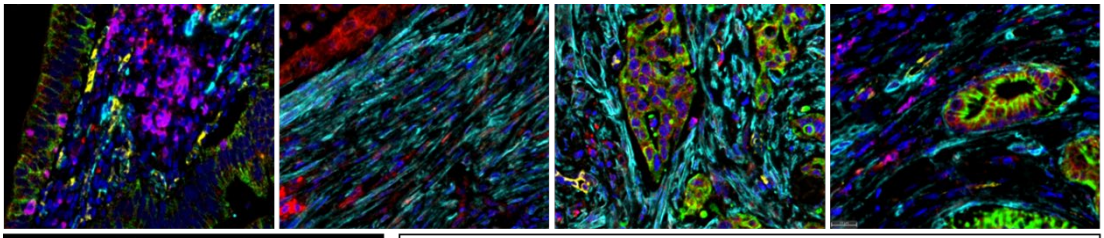


Figure 1: Multiplex Immunofluorescence showing large numbers of Cancer Associated Fibroblasts in pancreatic cancer tissue

Project Title: Examining the Surfaceome of Brain Cancer Cells to develop novel therapeutics

Supervisor: Dr Angelica Merlot AMerlot@ccia.org.au
Dr Dong-Hun Bae DBae@ccia.org.au

Suitable for: Honours, Masters or PhD Students

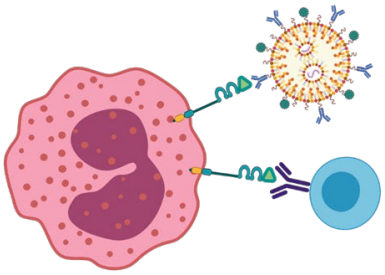
Project outline:

Importance of the project:

- Brain Cancer Kills more children than any other disease.
- New therapeutics are difficult to develop due to the Blood Brain Barrier.
- Cancer cell surface proteins are attractive targets due to their accessibility and dysregulated expression in cancer.
- In this project, we will uncover the cell surface protein targets on brain cancer cells and develop novel targeted nanoparticle anti-cancer therapeutics.

What the project will involve:

- The project will use a combination of techniques including biotinylating membrane proteins, mass spec, the use of patient tissue, orthotopic mouse models, nanoparticle development, molecular biology experiments, microscopy, etc.
- Feel free to contact Dr. Angelica Merlot to have a chat about whether the project matches your interests.



Targeting tumour surface proteins using tiny chemotherapeutic carrying nanoparticles or CAR T cells

Project Title: Targeting polyamines to eradicate the root of relapse in neuroblastoma

Supervisor: Dr Angelica Merlot AMerlot@ccia.org.au
Dr Dong-Hun Bae DBae@ccia.org.au

Suitable for: Honours, Masters or PhD Students

Project outline:

Importance of the project:

- Relapse is a major cause of cancer related death.
- Cancer Stem Cells can survive cancer therapeutics and restore the tumour to become more aggressive and resistant.
- Targeting polyamines that are upregulated in Cancer Stem Cells could eradicate this population, and therefore the root of relapse in neuroblastoma.

What the project will involve:

- This Project will determine the molecular mechanism of action of a novel polyamine inhibitor combination to eradicate cancer stem cells and how this compares to drugs currently used in the clinic.
- This will involve the use of patient tissue, western blotting and/or qPCR, cell viability assays and clonogenic assays.

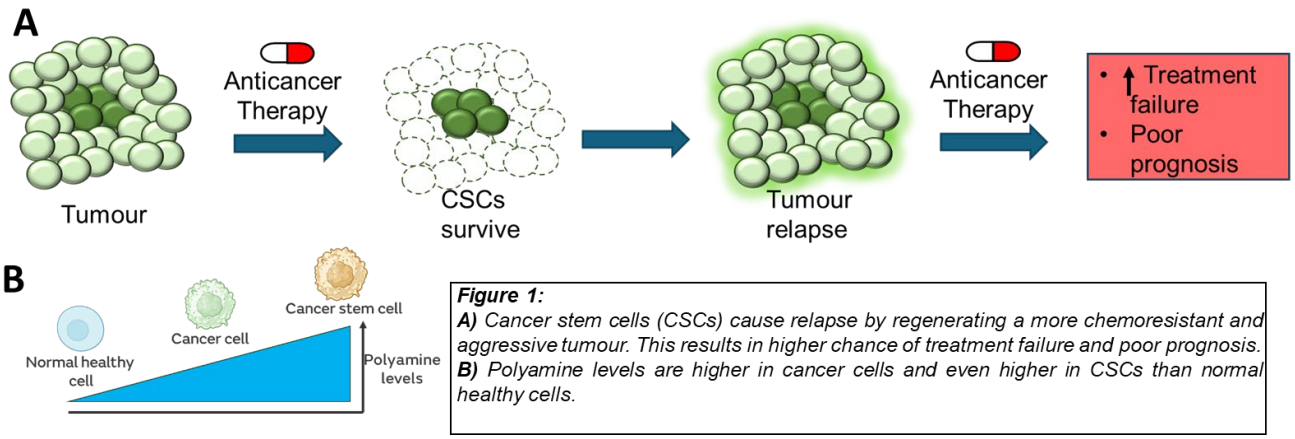


Figure 1:
A) *Cancer stem cells (CSCs) cause relapse by regenerating a more chemoresistant and aggressive tumour. This results in higher chance of treatment failure and poor prognosis.*
B) *Polyamine levels are higher in cancer cells and even higher in CSCs than normal healthy cells.*

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EMBRYONAL CANCER THERAPY & PREVENTION STUDENT PROJECTS

Project Title: **Effective targeting of chemoresistant subclones identified by single cell transcriptomics for the treatment of sarcomas**
Supervisor: A/Prof Belamy Cheung BCheung@ccia.org.au, Dr Parisa Ferdowsi PVahidi@ccia.org.au
Suitable for: Honours, Masters or PhD Students
Project outline:

Most child, adolescent and young adult (AYA) sarcoma patients achieve clinical remission with a "one-size-fits-all" chemotherapy approach based on histo-type. Almost one third will relapse and most will die of cancer. There is an urgent need for accurate assays which predict relapse. Longitudinal studies reveal minor cancer subclones at diagnosis which survive early chemotherapy, later leading to relapse. The precision of single cancer cell RNA sequencing (scRNA-seq) has provided unprecedented resolution to uncover the transcriptomic features of these minor subclones. At Children's Cancer Institute we have established the high-throughput droplet-single cell sequencing platform and have performed proof-of-principle experiments comparing osteosarcoma samples before and after chemotherapy, which indeed revealed enrichment of chemoresistant clones with sensitivities to drugs not normally used in that disease. Our study combines cutting edge scRNA-seq and whole exome sequencing (WES), advanced bioinformatics, large public datasets, and unique clinical resources to address fundamental questions about the impact of chemotherapy-resistant subclones on individual patient outcomes.

Techniques and key outcomes /learnings:

The Higher Degree Research Candidate will master cutting edge cellular and molecular techniques to test hypotheses that changes in genomic and transcriptomic patterns among residual malignant cells in the early phases of chemotherapy indicate subclonal selection for chemoresistance and relapse in patients, some techniques will include:

1. Single cell RNA sequencing and development of drug combinations.
2. Forward genetics using gene overexpression, knockdown and knockout.
3. Cellular and molecular techniques including flow cytometry, RT-PCR and immunoblotting.
4. Experience in working with patient-derived xenograft models of sarcoma.
5. Bioinformatics

Project Title: **Therapeutic and preventative strategies for children with high-risk neuroblastoma: targeting high fat diet-related metabolism**
Supervisor: A/Prof Belamy Cheung BCheung@ccia.org.au, Dr Ritu Mittra RMittra@ccia.org.au
Suitable for: Honours, Masters or PhD Students

Project outline:

Amongst the most aggressive and treatment-refractory childhood malignancies is high-risk neuroblastoma (NB). Whilst the survival of high-risk NB patients has improved over time, relapse rates in high-risk NB remain high at 50-60% with 5-year survival rates being less than 50% for these patients. Considerable evidence suggests that NB begins in embryonal neuroblasts indicating an aetiological relationship between NB tumorigenesis and embryonal environmental factors. Some studies have suggested that maternal obesity and high birth weight are risk factors for childhood cancer. We found that neuroblastoma driven by the MYCN proto-oncogene, originates from embryonal precancer cells persisting postnatally due to the loss of the normal death response. We discovered a drug which specifically restored the death response to these persistent embryo cells without affecting normal cells, and reduced tumour initiation in mouse models of child cancer. This drug appears to work by blocking cholesterol metabolism in the embryonal precancer cells. This research project will investigate a mechanistic understanding of how high fat diet, maternal obesity and high birth weight contribute to the aetiology of childhood cancer initiation and development and will enable development of effective agents for intervention during pregnancy or in early life that may reduce the incidence of childhood cancer.

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Techniques and key outcomes /learnings:

The Higher Degree Research Candidate will master cutting edge cellular and molecular techniques to test hypotheses that high fat diet-induced maternal obesity and high birthweight accelerates NB initiation by activation of fatty acid metabolism, leading to suppression of anti-tumour immunity, some techniques will include:

1. Therapeutic targets and drug identifications.
2. Molecular techniques using gene overexpression, knockdown and knockout.
3. Developing cancer prevention strategies.
4. Experience in working with transgenic and xenograft animal models.

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EXPERIMENTAL THERAPEUTICS AND MOLECULAR ONCOLOGY STUDENT PROJECTS

The aim of the Experimental Therapeutics Group is to develop more effective, targeted treatments for neuroblastoma – a cancer of embryonal neural crest cells and the most common solid tumour of early childhood. Children with neuroblastoma often present with advanced disease, and even with intensive therapies, many do not survive.

Most cancer chemotherapeutics are also highly toxic to normal tissues. Because of this lack of specificity, many childhood cancer survivors experience serious health problems in adulthood. There is an urgent need for targeted drugs with a high specificity for cancer cells and low toxicity for the normal growing tissues of a child.

Developing targeted treatments requires the identification and validation of molecular targets, and the technology and capability to translate that knowledge into drug discovery, preclinical testing, and clinical trials. This is the focus of our group. We use a variety of techniques including primary cell culture, cytotoxic assays, drug screening, drug testing in mice, genomic and transcriptomic analyses, histopathology and tissue microarray.

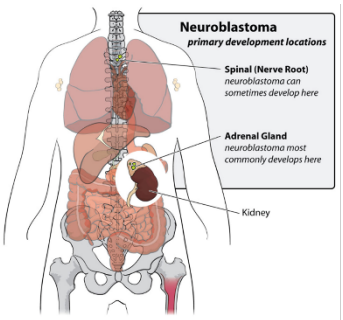


Figure 1. Primary development locations of neuroblastoma

Project Title: Establishment of clinically relevant neuroblastoma models

Supervisor: A/Prof Jamie Fletcher jfletcher@ccia.org.au; Dr Alvin Kamili akamili@ccia.org.au

Suitable for: Honours Students

Project outline:

Well characterised, high-quality preclinical models that realistically represent cancer patients are essential for translational research. Such models include patient-derived xenograft (PDX) and patient-derived cell line (PDCL) models. PDX models are established by direct engraftment of patient tumours into immunocompromised mice (Figure 2A). PDX models can represent the molecular diversity of cancers and can reproduce patient responses to anticancer agents. Our team has successfully established >40 models of high-risk neuroblastoma and use these models to support translational studies. As PDX models are resource intensive, time-consuming and animal-based, we are also developing alternative models for personalised medicine and translational research, including organoids models (Figure 2B).

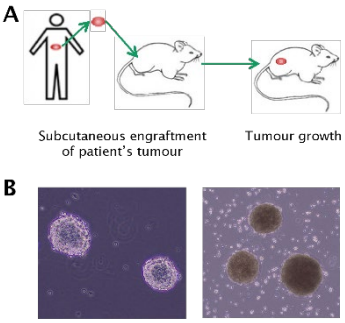


Figure 2. Patient-derived xenograft (A), and organoid (B) models

Project Title: Identifying synergistic combination therapy for venetoclax in neuroblastoma

Supervisor: A/Prof Jamie Fletcher jfletcher@ccia.org.au; Dr Alvin Kamili akamili@ccia.org.au;

Suitable for: Honours Students

Project outline:

Venetoclax is a relatively new drug that is proving effective against a range of cancers. Our initial studies suggest that venetoclax may also be effective against some high-risk neuroblastomas, however the experience with adult cancers suggests that combination therapy is likely to be more effective. Our study is focussed on identifying effective combinations with venetoclax and subjecting these combinations to rigorous preclinical testing in panel of patient-derived laboratory models of neuroblastoma. The study is designed to generate the evidence required to support subsequent clinical trials and has potential to directly impact on survival rates.

Project Title: Pre-emptive targeted therapy to optimise high-risk neuroblastoma treatment

Supervisor: A/Prof Jamie Fletcher jfletcher@ccia.org.au; Dr Alvin Kamili akamili@ccia.org.au; Dr Jayne Murray jmurray@ccia.org.au

Suitable for: Honours, Masters or PhD Students

Project outline:

Nearly 50% of children diagnosed with high-risk neuroblastoma still experience relapse or have refractory disease, for which there is no cure. Despite numerous early phase clinical trials, overwhelmingly conducted in

relapsed/refractory patients, their outcome remains especially poor, and <10% survive beyond 5 years.

The current treatment paradigm, where patients receive targeted/experimental therapies after failing standard-of-care treatment, is clearly inadequate, with potentially active treatments being introduced too late to meaningfully improve survival. In relapsed/refractory neuroblastoma, recurrent mutations have been identified in >50% tumours, with mutations concentrated in a small number of pathways, including RAS-MAPK, ALK, FGFR and P53/MDM2, suggesting that activation of a limited number of pathways allows HR-NB to survive non-targeted, cytotoxic chemotherapy. In this study, we are generating robust pre-clinical evidence to demonstrate the impact of earlier, pre-emptive intervention with targeted agents in clinically relevant, patient-derived models of newly diagnosed, untreated neuroblastoma.

Project Title: Understanding and targeting retrotransposons in childhood neuroblastoma

Supervisor: A/Prof Jamie Fletcher jfletcher@ccia.org.au; Dr Alvin Kamili akamili@ccia.org.au; Dr Jayne Murray jmurray@ccia.org.au

Suitable for: Honours or PhD Students

Project outline:

Much of the human genome consists of highly repetitive DNA originating from self-propagating sequences, with new transposition events dominated by long interspersed element-1 (LINE-1) activity. LINE-1 is an autonomous retrotransposon, meaning that it encodes its own protein machinery for reverse transcription and integration into the genome. While highly abundant (17% of the genome), only limited copies of LINE-1 can propagate, with the vast majority incomplete or mutated. Functional copies are repressed by epigenetic silencing, DNA repair, and host defence mechanisms. In adult cancer, LINE-1 can be de-repressed, contributing to genomic and epigenomic instability and tumour progression (Figure 3).

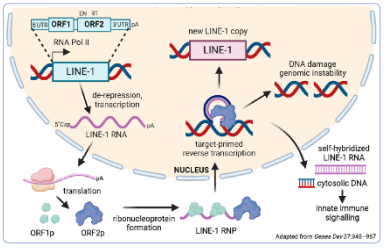
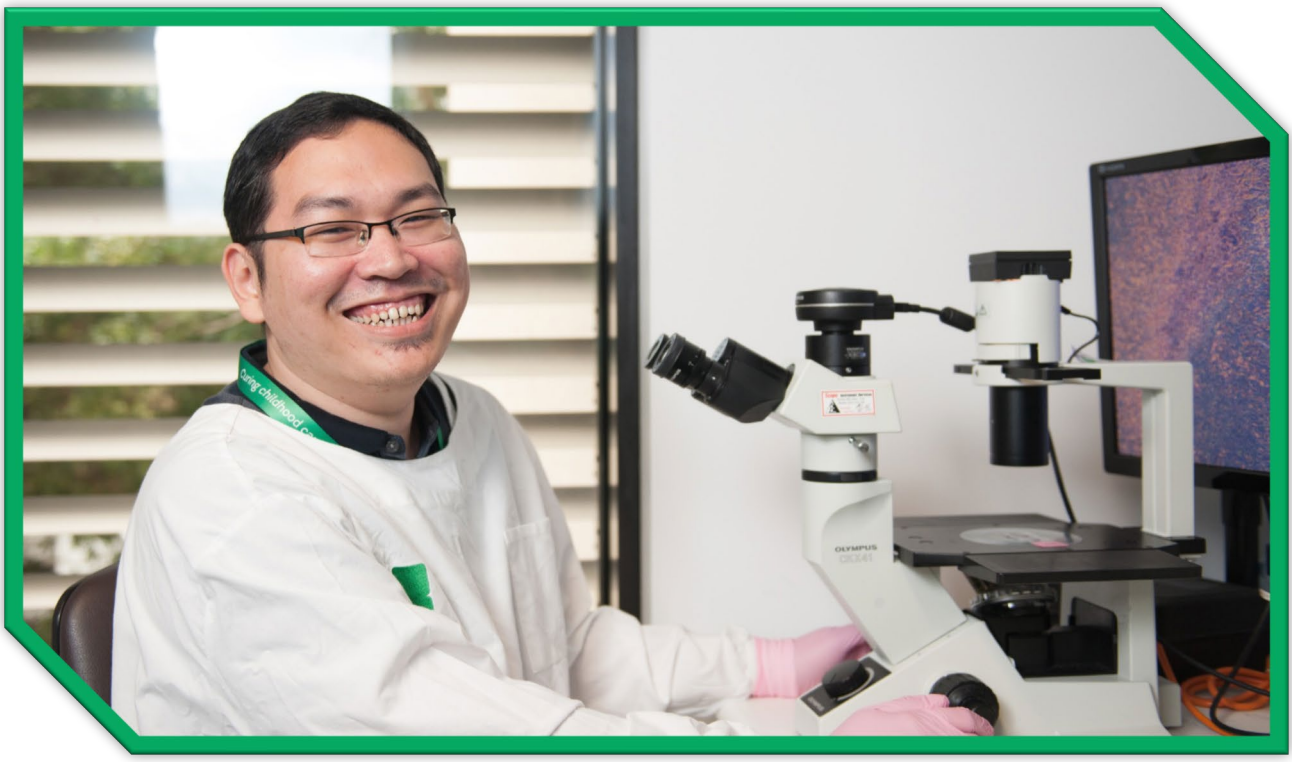


Figure 3. Life cycle of LINE-1 retrotransposons

This study will provide insights into the landscape of LINE-1 activity in neuroblastoma and will assess the activity of reverse transcriptase inhibitors to prevent tumour progression.



LEUKAEMIA BIOLOGY STUDENT PROJECTS

Project Title: **Nanomedicine for the targeted treatment of childhood leukaemia**
Supervisor: Prof Richard Lock RLock@ccia.org.au, Dr Narges Bayat NBayat@ccia.org.au; Dr Sara Mohamed smohamed@ccia.org.au
Suitable for: Honours, ILP, Masters or PhD Students
Project outline:

Acute lymphoblastic leukaemia (ALL) is the most common paediatric malignancy, and is one of the leading causes of death from disease in childhood. Progress in chemotherapy treatment has dramatically improved the survival rates of children with leukaemia. However, conventional therapeutic agents have inherent limitations such as low solubility, limited diffusion across cancer cell membranes, and low therapeutic index which leads to lower treatment efficiency. Moreover, the lack of target specificity of chemotherapy drugs leads to debilitating side effects in >60% of childhood cancer survivors. This highlights the importance of targeted delivery of drugs to cancer cells to ensure reduced toxicity on normal cells and a more efficient treatment. In this project we aim to integrate cancer biology and nanotechnology in order to develop a novel targeted diagnostic and therapeutic system to improve the efficacy, as well as to reduce side effects of chemotherapy treatment in childhood ALL.

Students will have access to the exceptional technical resources, equipment and facilities of the laboratories of Children's Cancer Institute. Some of the techniques and resources involved in this project may include molecular biology, conducting cytotoxicity and cell viability assays, studying cellular interactions of antibodies with their specific targets and preclinical testing of novel therapeutics in orthotopic patient derived xenograft mouse models of childhood ALL.

Project Title: **Liquid biopsy for monitoring of minimal residual disease in childhood acute leukaemia**
Supervisor: Prof Richard Lock RLock@ccia.org.au, Dr Narges Bayat NBayat@ccia.org.au
Suitable for: Honours, ILP, Masters, or PhD Students

Project outline:

Acute lymphoblastic leukaemia (ALL) is the most common childhood cancer. Around 20% of ALL patients will eventually relapse and the prognosis for these patients remains as low as 30%. The strongest prognostic factor for relapse and poor prognosis in childhood ALL is the persistence of minimal residual disease (MRD) in the bone marrow throughout therapy. The current gold standard for detecting MRD and early relapse in high-risk childhood leukaemia are patient- specific tests performed on bone marrow samples collected from the patient. We aim to develop less invasive, but equally sensitive, methods to detect MRD in the peripheral blood called "liquid biopsy". Liquid biopsy is the detection of DNA or microRNA (miRNA) fragments released into the blood and bone marrow by cancer cells (circulating tumour DNA [ctDNA] or ct-miRNA). However, there is limited information about liquid biopsy in childhood leukaemia. Therefore, this project aims to investigate if liquid biopsy can be used for the sensitive detection of residual leukaemia and whether it can be used for ALL risk stratification analogous to conventional MRD assays. Some of the techniques and resources involved in this project may include: Orthotopic patient derived xenograft mouse model of childhood ALL which is considered to be the most clinically relevant model to assess novel therapeutics and diagnostic approaches for childhood leukaemia.

Project Title: **Therapeutic targeting of T-cell acute lymphoblastic leukemia using an AKR1C3 activated prodrug**
Supervisor: Prof Richard Lock RLock@ccia.org.au, Dr Charles de Bock CDeBock@ccia.org.au
Suitable for: Honours, Masters or PhD Students
Project outline:

Acute lymphoblastic leukaemia (ALL) is the most common paediatric malignancy and can be broadly divided into B-lineage (B-ALL) and T-lineage (T-ALL). T-ALL is an aggressive malignancy that is exceptionally difficult to cure after

relapse. We have recently shown that T-ALL expresses significantly higher levels of the enzyme AKR1C3 compared with B-ALL. These findings were exploited using a first-generation AKR1C3-activated prodrug, OBI-3424, now in a clinical trial.

Our initial testing of the second-generation AKR1C3-activated prodrug, ACHM-025, has shown greater selectivity for activation by AKR1C3 and superior antileukemic efficacy compared with OBI-3424. Moreover, we have identified two active downstream AKR1C3 enhancer regions in T-ALL versus B-ALL cells. In this project we aim to understand the mechanism of AKR1C3 regulation in T-ALL versus B-ALL, and test the efficacy of ACHM-025. This work will facilitate the development of ACHM-025 and will lead to personalised approaches to improve the outcome for patients with T-ALL.

Aims of the project:

1. Define the determinants of response to AKR1C3-activated prodrugs.
2. Define the mechanism of AKR1C3 gene regulation in T-ALL versus B-ALL.
3. Test the in vivo efficacy of ACHM-025 alone and in combination with standard-of-care drugs.

This research project incorporates both discovery science and preclinical studies and will involve molecular biology, epigenetics, genomics and in vivo preclinical testing in our patient-derived xenograft model of paediatric ALL.

Project Title: **Targeted treatments for high-risk acute lymphoblastic leukaemia in children**
Supervisor: Prof Richard Lock ✉ RLock@ccia.org.au, Dr Patrick Connerty ✉ PConnerty@ccia.org.au
Suitable for: Honours, Masters or PhD Students

Project outline:

Acute lymphoblastic leukaemia (ALL) is the most common paediatric malignancy and, despite marked improvements in treatment over the past 60 years, it remains one of the most common causes of death from disease in children. While most children will experience good outcomes, several high-risk ALL subtypes, as well as children who experience relapse from their disease, require the development and testing of novel targeted treatments to facilitate cure.

This student project is part of a larger preclinical drug testing endeavor funded in the Primary Supervisor's lab by the US National Cancer Institute continuously for 21 years. Novel targeted drugs are selected for testing in patient-derived xenograft models of paediatric ALL, in collaboration with industry partners. The most active agents are then prioritised for advanced testing and for progression into clinical trials. Several opportunities exist to further elucidate the mechanisms of action of these active drugs, and the molecular determinants of sensitivity or resistance, using cutting edge cell and molecular techniques.

Techniques and key outcomes /learnings:

The Higher Degree Research Candidate will master cutting edge cell and molecular techniques to test hypotheses relating to anti-leukaemic drug mechanism of action and determinants of in vivo sensitivity or resistance, some of which will include:

1. Forward genetics using gene overexpression, knockdown and knockout
2. Genome-wide and small library CRISPR/Cas screening in vitro and in vivo
3. Cell and molecular techniques including flow cytometry, RT-PCR and immunoblotting
4. Experience in working with patient-derived xenograft models of acute leukaemia

CHILDREN'S CANCER INSTITUTE

Project Title: **Identifying novel long non-coding RNAs vital for paediatric acute myeloid leukemia**

Supervisor: Dr Patrick Connerty PConnerty@ccia.org.au, Prof Richard Lock RLock@ccia.org.au

Suitable for: PhD Students

Project outline:

Acute myeloid leukaemia (AML) is a haematological cancer with dismal survival rates in children. A major limitation of AML treatment is the off-target toxicity of current chemotherapies. Consequently, there is a need to identify molecular targets which are specific to AML and absent in healthy cells, allowing for a precision medicine approach to treat the disease. Long non-coding RNAs (lncRNAs) are a class of RNAs which have unique expression profiles in multiple cancers, including AML. Targeting lncRNAs therapeutically is a rapidly emerging field and presents an opportunity to specifically eradicate AML cells. Therefore, the aims of this project are to identify lncRNAs that are both specific and vital for AML cells and explore their potential as therapeutic targets.

Techniques and key outcomes /learnings:

- Tissue culture
- RNA extraction
- qPCR
- Flow cytometry
- Transfection
- Viral transduction
- CRISPR-Cas9 screening
- Bioinformatic analysis
- Animal studies (mice)
- Project design
- Manuscript writing

CHILDREN'S CANCER INSTITUTE

MOLECULAR DIAGNOSTICS STUDENT PROJECTS

Project Title: **Molecular Diagnostics for Children with Acute Lymphoblastic Leukaemia**

Supervisor: Dr Michelle Henderson ✉ MHenderson@ccia.org.au,
Dr Toby Trahair ✉ Toby.trahair@health.nsw.gov.au

Suitable for: Honours, ILP or Masters Students

Project outline:

In acute lymphoblastic leukaemia (ALL), the amount of malignant cells that remain in the bone marrow after chemotherapy, referred to as minimal or measurable residual disease (MRD), is highly prognostic of clinical outcome. Molecular monitoring of MRD during treatment is widely used to help predict relapse and to tailor therapy for individual patients. These analyses typically involve quantitative PCR based on leukaemia-specific IG/TCR gene rearrangements for each patient, but these are time-consuming to develop and not achievable for all patients.

Recent technological developments provide opportunities to improve the coverage and quality of molecular PCR-based MRD testing. Several projects are available:

1) A newly developed in-house software for identification of IG/TCR rearrangements from next-generation whole genome sequencing (WGS) data will be compared to traditional approaches.

2) WGS data will be used to identify alternative genomic breakpoints (other than IG/TCR genes) that can be used to design robust leukaemia-specific qPCR-based tests.

For 1) and 2), performance of each assay designed will be evaluated against the current MRD monitoring procedures using material available through the CCI tumour bank.

3) To most efficiently apply WGS for MRD monitoring, it would be ideal to be able to predict up-front which patients are more likely to fail conventional MRD marker development. Based on a hypothesis that this property might be influenced by the biology of the disease, clinicopathological and genetic data will be used to develop machine learning algorithms to help identify such cases.

4) Very low level MRD is of increasing clinical interest, especially for patients receiving bone marrow transplants or immunotherapies. We are investigating approaches to improve assay sensitivity and to distinguish true positive results.

CHILDREN'S CANCER INSTITUTE

SARCOMA BIOLOGY AND THERAPEUTICS STUDENT PROJETS

Project Title: Discovering actionable drug targets for young patients with sarcoma through phosphoproteomics

Supervisor: Dr Emmy Fleuren efleuren@ccia.org.au

Suitable for: Honours, Masters or PhD Studies

Project outline:

Sarcomas are a diverse group of highly aggressive tumours that disproportionally affect the young. Despite aggressive treatments, survival is limited (~20% in advanced setting) and side-effects frequently occur, stressing the unmet need to identify better and kinder treatments. Pinpointing clinically actionable targets is however extremely challenging in these tumours. Although genomic data interrogation has revolutionised cancer therapies, it often does not identify a targeted treatment for young sarcoma patients.

Tumour genomics are however only one piece of the puzzle, and the picture they paint is incomplete. Our team has generated compelling data that when we couple a phosphoproteomics approach (to identify novel and activated drug targets at the protein level) to a robust preclinical functional validation framework (where we test *in vitro* and *in vivo* if drugs that 'switch off' those newly identified targets truly inhibit sarcoma growth), this can aid clinical decision-making. Our earlier phosphoproteomic discovery already influenced clinical drug recommendations for selected young sarcoma patients, where a young patient had tumour shrinkage while treated with a novel drug our team recommended. Now, more research is needed to make new drugs a treatment reality for more young sarcoma patients.

We have an excellent opportunity for a PhD/Honours student to join our young and dynamic team and dive into this project. You will study the phosphorylation patterns in sarcoma patient samples, aiming to identify novel, clinically actionable targets for young sarcoma patients that are currently missing out. You will work closely with the ZERO Childhood Cancer program (ZERO), which is Australia's nationwide precision medicine program aimed to identify a personalised, targeted treatment for all children with cancer (including those with sarcoma). You will use a variety of molecular methodologies, including Mass-Spectrometry and targeted phosphoproteomic assays (e.g. Kinome Profiler/Western Blot/Immunohistochemistry). Functional relevance of identified targets will be validated using *in vitro* (drug screens/siRNA/CRISPR) and *in vivo* (drug efficacy) sarcoma models; exact techniques depend on Honours/PhD level.

Results have the potential to have a clinical impact on sarcoma patients in ZERO.

CHILDREN'S CANCER INSTITUTE

TRANSLATIONAL TUMOUR BIOLOGY STUDENT PROJECTS

Project Title: **Integrative data analysis: from novel biomarker-drug response associations to predicting effective drug combinations**

Supervisor: Dr Emmy Dolman ✉ EDolman@ccia.org.au; A/Prof Paul Ekert ✉ PEkert@ccia.org.au

Suitable for: Honours, or PhD Students

Project outline:

More than 140 children with cancer die in Australia each year due to the occurrence of resistance to traditional chemotherapy. To improve overall survival rates for high-risk paediatric cancer patients, Children's Cancer Institute initiated the Zero Childhood Cancer national personalised medicine trial (PRISM). Within this trial, tumour biopsies from children with high-risk cancer are collected for full molecular profiling to identify cancer driver events and for the generation of patient-derived model systems to link these events to targeted therapies.

WGS, RNA-Seq and DNA methylation profiling of >350 tumour samples showed actionable events in only 70% of the patients. High-throughput drug testing on >150 patient-derived samples yielded unexpected efficacy patterns for single agent targeted drugs without an associated predictive biomarker, but clinical trials for paediatric cancer have proven that treatment with single agents is insufficient in most cases. The current study aims to integrate PRISM molecular profiling and in vitro drug efficacy datasets to identify novel biomarker-drug response associations and predict effective drug combinations for paediatric cancer by developing novel bioinformatic algorithms. Publicly available databases such as DepMap, CancerrXGene and NCI-ALMANAC that contain in vitro efficacy data for single drugs and drug combinations alongside molecular characterisation of the used model systems will be exploited for algorithm optimisation and deeper integrative analysis. Novel discovered biomarker-drug response associations and drug combinations will be validated in vitro and in vivo in patient-derived model systems to guide future clinical trials for paediatric cancer treatment.

Project Title: **Novel drug combination bullets for improved targeting of oncogenic signaling pathways driving high-risk paediatric cancer**

Supervisor: Dr Emmy Dolman ✉ EDolman@ccia.org.au; A/Prof Paul Ekert ✉ PEkert@ccia.org.au

Suitable for: Honours, or PhD Students

Project outline:

More than 140 children with cancer die in Australia each year due to the occurrence of resistance to traditional chemotherapy. The global effort to understand the molecular basis of high-risk paediatric cancers has unravelled several important signaling pathways frequently genetically altered, including Ras-MAPK, PI3K-Akt-mTOR, cell cycle, and DNA damage response. This has led to the clinical use of drugs targeting selective key players in these pathways such as trametinib inhibiting the Ras-MAPK key player MEK. However, clinical responses to many targeted drugs have been disappointing because of 1) the challenge to accurately predict which patients might benefit from targeted therapies
and 2) the occurrence of resistance to single targeted drugs. The current study aims to identify improved predictive biomarkers and combination strategies to overcome resistance for clinically available drugs targeting key oncogenic signaling pathways driving high-risk paediatric cancers. We will make use of the unique resources available through the national Zero Childhood Cancer personalised medicine program, including WGS and RNA sequencing data for >600 tumour samples, in vitro drug response data for >150 tumour samples, and >150 patient-derived models. Biomarker identification and validation will be performed using technologies such as integrative data analysis, phosphoproteomics, and CRISPR gene editing. Novel drug combinations will be identified by in vitro high-throughput combination testing and genome-wide CRISPR screening. Novel discovered biomarker-drug response associations and drug combinations will be validated in vitro and in vivo in patient-derived model systems to guide future clinical trials for paediatric cancer treatment.

CHILDREN'S CANCER INSTITUTE

Project Title: **Unlocking the full potential of personalised treatments – investigating novel mechanisms of kinase activation in paediatric cancer**

Supervisor: Dr Lauren Brown LBrown@ccia.org.au and A/Prof Paul Ekert PEkert@ccia.org.au

Suitable for: PhD Students

Project outline:

Personalised medicine programs like the Zero Childhood Cancer Program (ZERO) analyse individual patient tumours to identify molecular targets for therapy. Receptor tyrosine kinases (RTKs) can be effectively targeted with RTK inhibitors when activated in cancer, most notably by gene fusions and missense mutations. The challenge arises when genomic alterations are identified in RTK genes but the functional consequences (whether the alteration results in RTK activation and RTK inhibitor sensitivity) of the alteration are unknown. Through functional analysis of individual genomic alterations in RTK genes we have characterised novel mechanisms of kinase activation, identifying more patients that will benefit from RTK inhibitor therapy.

In this project, we will investigate a range of novel and suspected kinase-activating genomic events identified in ZERO. Examples of these events include:

1. Novel structural variants involving RTK genes
2. Alternative splicing of RTK genes
3. Mutation of RTK regulating genes

We will use well-established ectopic overexpression systems and CRISPR/Cas9 for gene knockout, as well as emerging genomic and RNA editing techniques, including CRISPR activation (CRISPRa) and CRISPR/Cas13, to generate accurate cell models of individual variants. We will then use molecular and cell biology techniques to characterise the capacity to drive cellular transformation, the molecular mechanisms by which the variant drives transformation, and sensitivity to targeted inhibitors.

By functionally characterising individual genomic variants, this project will enhance our understanding of RTK biology in cancer and importantly, identify a new class of patients that may benefit from RTK inhibitors.

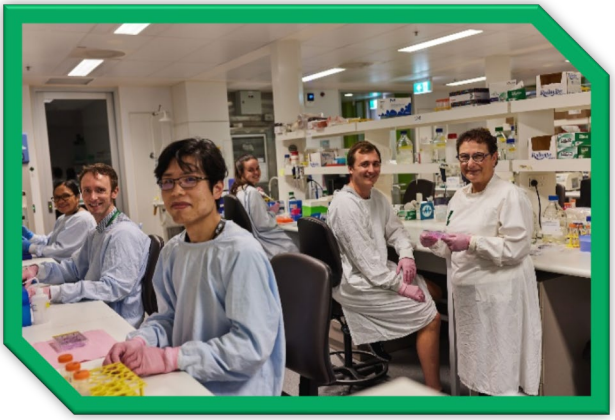
TUMOUR BIOLOGY AND TARGETING GROUP STUDENT PROJECTS

Project Title: **Engineering childhood cancer models for precision medicine**
Supervisor: Prof Maria Kavallaris ✉ MKavallaris@ccia.org.au
Dr Valentina Poltavets ✉ VPoltavets@ccia.org.au
Suitable for: Honours, Masters or PhD Students

Project outline:

Neuroblastoma and sarcoma patients with recurrent and drug resistant disease have less than a 30% chance of survival and limited therapeutic options. Preclinical models hold a great promise in improving personalised medicine approaches and as a result - patient outcomes. Our laboratory is using 3D bioprinting technology to create culturing conditions for patient-derived cancer cells that mimic native tumour microenvironments.

The extracellular matrix (ECM) is an important component of the tumour microenvironment. However, its roles in childhood solid tumours are not well characterised. Initial gene expression analysis indicates that specific ECM genes are abundantly expressed in these tumours. This project aims to investigate the ECM proteins in patient tissue samples as well as to understand the connection between protein expression and patient survival. The impact of these ECM proteins on the tumour growth will be evaluated by establishing and investigating mini-tumours in a dish using advanced 3D bioprinting technology. This exciting project will contribute to developing predictive preclinical models of childhood cancers and improve therapy for high-risk paediatric cancer patients.



Project Title: **Investigating immune cell reprogramming mRNA nanotherapeutics in immunocompetent models of paediatric brain and neuronal cancers**
Supervisor: Dr Ernest Moles ✉ EMoles@ccia.org.au, Prof Maria Kavallaris ✉ MKavallaris@ccia.org.au, and Dr Maria Tsoli ✉ MTsoli@ccia.org.au
Suitable for: Honours, Masters or PhD Students

Project outline:

Cancers originating in the brain and peripheral nerves, such as diffuse midline gliomas and high-risk neuroblastoma, are among the most aggressive cancers during childhood. Chemotherapy and radiotherapy have been vastly unsuccessful, and there is an urgent need to develop safer and more potent treatment strategies for these cancers.

Herein, the student will participate in an innovative and multidisciplinary project whereby we aim to redirect the immune response in the patient, using injectable messenger RNA nanoparticles, to identify and eliminate the cancer cells. Moreover, this treatment approach will be investigated in advanced murine models of brain cancer and high-risk neuroblastoma that harbour an intact functional immune system and closely resemble the behaviour and pathophysiology of human disease.

The student will learn innovative tools and acquire knowledge in cancer biology, cellular therapy, and mRNA nanomedicine to advance the next generation of therapeutics to fight the deadliest of all paediatric cancers.

Join Our Team

Cancer cuts life short for hundreds of children in Australia every year, before they've even had a chance to make their mark. You can help change that. Be part of a team that is working tirelessly to find a cure for childhood cancer. A team that is working together every day to help children live longer and more fulfilling lives.

If you're interested in pursuing any of the projects listed above, please get in contact with the relevant research leader or visit the **CCI website** for more information.

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