2027

Student Projects

Children's Cancer Institute

UNSW SYDNEY

A Message from the Executive Director

Prof Louis Chesler
Children's Cancer Institute
Executive Director

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.

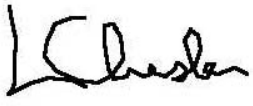
Children's Cancer Institute is the only independent medical research institute in Australia wholly dedicated to putting an end to childhood cancer. We use a multi-pronged approach to tackling childhood cancer by investigating causes and prevention, improving diagnosis and monitoring and developing more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

At the beginning of 2026, Children's Cancer Institute moved 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 brings 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.



Professor Louis Chesler Executive Director 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.

Facilities & Resources

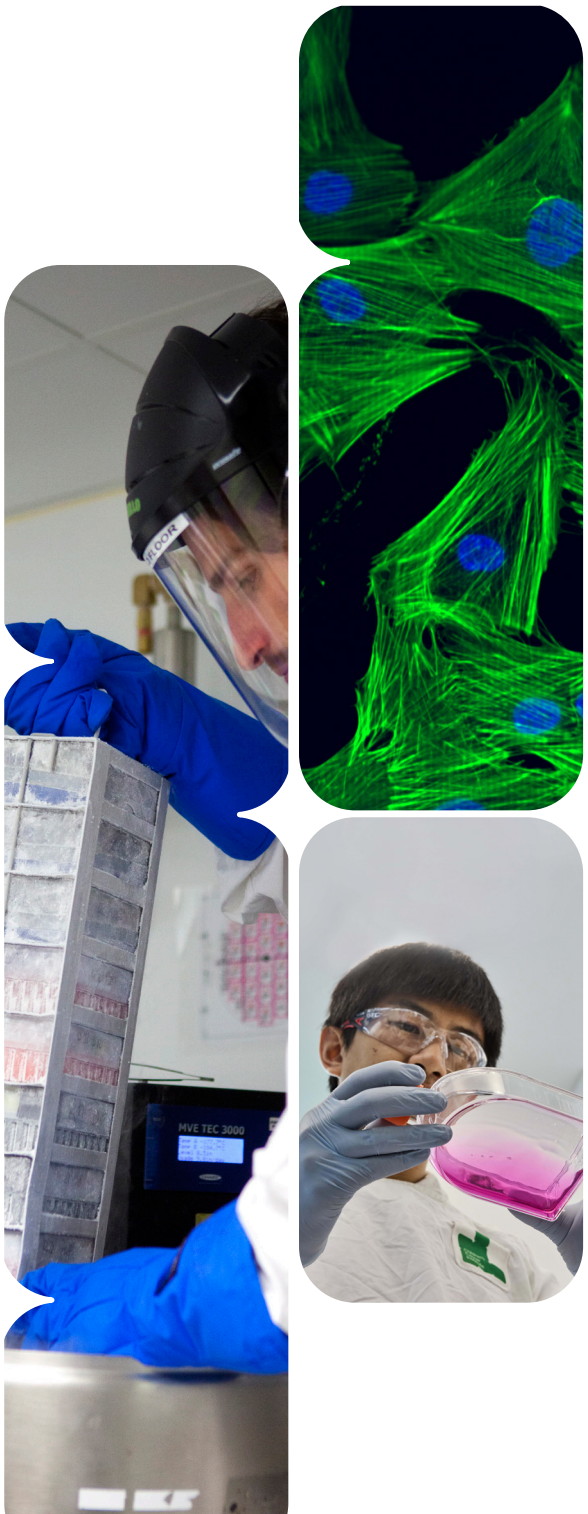
- State-of-the-art PC2 laboratories
- Core Services team to facilitate the efficient day-to-day operation of the labs
- Own animal facility, where expert staff provide researchers with training and advice
- Close relationship with clinicians at the Kids Cancer Centre (KCC), Sydney Children's Hospital, 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 3000 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.

Research Facilities, Platforms & Technologies

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.

Research Facilities, Platforms & Technologies

Platforms and Technologies:

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.

Minderoo Children's Comprehensive Cancer Centre

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.

As Australia's first children's comprehensive cancer centre, MCCCC includes:

- 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.

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 focused 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

The CCI Top Up is a scholarship Top-Up offered to full time Higher Degree Research students who have been awarded a competitive scholarship (usually from UNSW). The top up is additional to the scholarship stipend and they total $40,000p/a (tax free). The Top Up award supports living costs while studying.

Josh Mccarroll Memorial Phd Award

This competitive tax-free award, to a value of up to $10,000 AUD per annum, is offered to students demonstrating exceptionally high potential who have succeeded in attracting a primary competitive scholarship. The Josh McCarroll Memorial PhD 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 October 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 UNSW Sydney. 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 enroll 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/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

https://www.unsw.edu.au/science/student-life-resources/honours-how-apply

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. Associate Professor Michelle Henderson (mhenderson@ccia.org.au) is the School'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.

Cancer Biology
EMBRYONAL CANCER THERAPY AND PREVENTION GROUP
Prof Glenn Marshall - Group Leader
GMarshall@ccia.org.au

Cancer Biology
FUNCTIONAL GENOMICS OF LEUKAEMIA GROUP
A/Prof Charles de Bock - Group Leader
CDeBock@ccia.org.au

Cancer Biology
GENOMIC CHILDHOOD CANCER RISK GROUP
A/Prof Mark Pinese - Team Leader
MPinese@ccia.org.au

Cancer Biology
LEUKAEMIA BIOLOGY GROUP
Prof Richard Lock - Group Leader & Theme Head - Cancer Biology
RLock@ccia.org.au

Cancer Biology
TRANSLATIONAL TUMOUR BIOLOGY GROUP
Prof Paul Ekert - Group Leader and Deputy Director -Research Themes
PEkert@ccia.org.au

Clinical Translation
COMPUTATIONAL BIOLOGY GROUP
Prof Mark Cowley - Group Leader and Deputy Director -
Enabling Platforms and Collaboration
MCowley@ccia.org.au

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.

Clinical Translation
SARCOMA BIOLOGY AND THERAPEUTICS GROUP
A/Prof Emmy Fleuren - Team Leader
EFleuren@ccia.org.au

Clinical Translation
ZERO CHILDHOOD CANCER
A/Prof Vanessa Tyrrell - Program Director & Theme Head – Clinical Translation
vtyrrell@ccia.org.au

Therapeutic Discovery
BRAIN TUMOURS GROUP
Prof David Ziegler - Group Leader
DZiegler@ccia.org.au

Therapeutic Discovery
CANCER EPIGENETIC BIOLOGY AND THERAPEUTICS GROUP
A/Prof Fa Valdes Mora - Team Leader & Theme Head - Therapeutic Discovery
FValdesMora@ccia.org.au

Therapeutic Discovery
CHEMICAL BIOLOGY AND TARGET BASED THERAPIES GROUP
Dr Jean Bertoldo - Team Leader
JBertoldo@ccia.org.au

Therapeutic Discovery
COMPUTATIONALLY ENABLED DRUG DISCOVERY GROUP / THINK
A/Prof Antoine de Weck - Group Leader
ADeWeck@ccia.org.au

Research Groups

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Therapeutic Discovery
EXPERIMENTAL THERAPEUTICS & MOLECULAR ONCOLOGY GROUP
Prof Michelle Haber and Prof Murray Norris - Group Leaders
MHaber@ccia.unsw.edu.au & MNorris@ccia.org.au

Therapeutic Discovery
TRANSLATIONAL CANCER NANOMEDICINE GROUP
Prof Maria Kavallaris - Group Leader
MKavallaris@ccia.org.au

Therapeutic Discovery
CANCER TARGETS AND THERAPEUTICS GROUP
Dr Angelica Merlot - Research Fellow
AMerlot@ccia.org.au

Projects

Project Number	Project Name	Supervisors
CANCER BIOLOGY THEME		
EMBRYONAL CANCER THERAPY AND PREVENTION GROUP		
Project 1	A Systematic and Multi-Modal Framework to Identify and Target Metabolic Vulnerabilities Following Chemotherapy in Childhood Cancers	Dr Kenny Yeo A/Prof Belamy Cheung
Project 2	Therapeutic Targeting of Chemo resistant Subclones Identified by Single-Cell Transcriptomic Profiling in Sarcomas	Dr Parisa Vahidi Ferdowsi A/Prof Belamy Cheung
Project 3	A high-fat environment as a mechanism of initiation and progression of MYCN-driven medulloblastoma	Dr Ritu Mittra A/Prof Belamy Cheung
FUNCTIONAL GENOMICS OF LEUKAEMIA GROUP		
Project 4	CRISPR activation screening to identify resistance mechanisms for a new AKR1C3-activated pro-drug in TCF3::HLF-positive leukaemia.	Dr Hansen Kosasih A/Prof Charles De Bock
LEUKAEMIA BIOLOGY GROUP		
Project 5	Developing novel targeted therapeutics for the treatment of paediatric acute lymphoblastic leukaemia	Dr Sara Mohamed Prof Richard Lock
Project 6	Evaluating novel therapeutics for treating paediatric acute myeloid leukaemia	Dr Patrick Connerty Prof Richard Lock
Project 7	Investigating the role of long non-coding RNAs in paediatric acute myeloid leukaemia	Dr Patrick Connerty Prof Richard Lock
TRANSLATIONAL TUMOUR BIOLOGY GROUP		
Project 8	Integrative data analysis: from novel biomarker-drug response associations to predicting effective drug combinations	Dr Emmy Dolman Jie Mao
Project 9	Novel drug combination bullets for improved targeting of oncogenic signaling pathways driving high-risk paediatric cancer	Dr Emmy Dolman
Project 10	The Functional Genomics of Molecular Targets in Paediatric Cancer	A/Prof Paul Ekert Dr Pei Liu
Project 11	Genome-wide CRISPR Screening to Identify Dependencies in High-Risk Paediatric Cancer	Dr Hansen Kosasih Prof Paul Ekert
CLINICAL TRANSLATION THEME		
COMPUTATIONAL BIOLOGY GROUP		
Project 12	The onco-mitochondrial landscape of childhood cancer	Dr Piyushkumar Mundra Prof Mark Cowley
Project 13	Transcriptomic analysis of locus specific LINE-1 activity in paediatric cancer	Dr Nandan Deshpande
SARCOMA BIOLOGY AND THERAPEUTICS GROUP		
Project 14	Discovering actionable drug targets for young patients with sarcoma through phosphoproteomics	A/Prof Emmy Fleuren
Project 15	Finding better and kinder treatments for young patients with osteosarcoma and beyond	A/Prof Emmy Fleuren

Project Number	Project Name	Supervisors
THERAPEUTIC DISCOVERY THEME		
BRAIN TUMOURS GROUP		
Project 16	Exposing the enemy: epigenetic therapy reveals hidden viral passengers with oncogenic potential in DIPG	Dr Benjamin Rayner Prof David Ziegler
Project 17	Discovery and evaluation of novel targeted drug combinations for aggressive paediatric ependymoma	A/Prof Maria Tsoli Yongjuan (Joan) Chen
Project 18	Developing therapies to overcome the high-lactic acid tumor environment induced in DMG	Dr Jessica Bell Prof David Ziegler
CANCER TARGETS AND THERAPEUTICS GROUP		
Project 19	Specific Targeting of Tumour-Promoting Cancer-Associated Fibroblasts in Pancreatic Cancer	Dr Angelica Merlot Prof Minoti Apte
Project 20	Examining the Surfaceome of Brain Cancer Cells to develop novel therapeutics	Dr Angelica Merlot A/Prof Tushar Kumeria
Project 21	Targeting polyamines to eradicate the root of relapse in neuroblastoma	Dr Angelica Merlot Dr Klaartje Somers
CHEMICAL BIOLOGY AND TARGET BASED THERAPIES GROUP		
Project 22	Integrating data science, chemical biology, and basic biology to uncover the AML druggable proteome with small-molecule covalent ligands	Dr Jean Bertoldo
Project 23	Development of covalent ligand inhibitors for IGF2BP3	Dr Jean Bertoldo
Project 24	Development of covalent ligands as inhibitors of IPO4 for multiple cancers	Dr Jean Bertoldo
COMPUTATIONALLY ENABLED DRUG DISCOVERY GROUP / THINK		
Project 25	Functional validation of engineered U1 snRNAs targeting cancer-relevant poison exons	A/Prof Antoine de Weck Dr Pragya Gupta Dr Pablo Aceras Mateos
Project 26	Automating biology to accelerate AI-guided drug discovery	A/Prof Antoine de Weck AJ Sethi
Project 27	Reactivation of Tumour Suppressor Genes via RNA Splicing Engineering	Dr Trakansuebkul A/Prof Antoine de Weck
EXPERIMENTAL THERAPEUTICS & MOLECULAR ONCOLOGY GROUP		
Project 28	Pre-emptive targeted therapy to optimise high-risk neuroblastoma treatment	A/Prof Jamie Fletcher Dr Alvin Kamili Dr Jayne Murray
Project 29	Novel combination therapies for child, adolescent and young adult sarcoma	Prof Michelle Haber Prof Murray Norris A/Prof Jamie Fletcher Dr Jayne Murray
TRANSLATIONAL CANCER NANOMEDICINE GROUP		
Project 30	Engineering childhood cancer models for precision medicine	Prof Maria Kavallaris Dr Anna Guller
Project 31	Investigating immune cell reprogramming mRNA nanotherapeutics in immunocompetent models of paediatric brain and neuronal cancers	Dr Ernest Moles Prof Maria Kavallaris Dr Maria Tsoli
Project 32	Engineering Precision RNA Therapies for Childhood Cancer	Prof Maria Kavallaris Dr Amy Logan

Projects

EMBRYONAL CANCER THERAPY AND PREVENTION GROUP

Group Leader: Professor Glenn Marshall
Principal Scientist: A/Professor Belamy Cheung

PROJECT 1

Project Title: **A Systematic and Multi-Modal Framework to Identify and Target Metabolic Vulnerabilities Following Chemotherapy in Childhood Cancers**
Supervisor: Dr Kenny Yeo kyeo@ccia.org.au
A/Prof Belamy Cheung bcheung@ccia.org.au
Suitable for: Honours, ILP or PhD Students

Project outline:
Chemotherapy remains a cornerstone in the treatment of childhood cancers, yet its long-term effectiveness is limited by tumour relapse, resistance, and the emergence of secondary malignancies. Increasing evidence suggests that chemotherapy induces persistent alterations in tumour metabolism, which may create exploitable therapeutic vulnerabilities. This project will adopt a systematic and multi-modal approach to investigate metabolic changes that occur in childhood cancers following chemotherapy. The overarching goal is to identify conserved, targetable metabolic pathways that could be leveraged to improve treatment outcomes and reduce the risk of relapse.

The project will begin with a systematic review and meta-analysis of existing studies reporting chemotherapy-induced metabolic changes in paediatric tumours. Using standardised methodologies, this review will synthesise findings across both preclinical and clinical studies to provide a foundational map of chemotherapy-related metabolic reprogramming. Genomic and transcriptomic datasets identified through this review, together with our existing scRNA datasets, will then be analysed to uncover metabolic signatures characteristic of post-chemotherapy tumour states. Through integrative bioinformatics analyses, we will uncover key metabolic vulnerabilities and nominate candidate therapeutic targets that are consistently altered following chemotherapeutic exposure. These findings will be experimentally validated using our deconstructed chemotherapeutic model in vitro. Cancer cell lines will be exposed to clinically relevant chemotherapy agents, and resulting metabolic changes will be characterised. Functional assays will then be used to evaluate potential therapeutic vulnerabilities, including drug sensitivity screening and pathway inhibition. Finally, selected metabolic targets will be validated in vivo using xenograft or patient-derived models to assess their therapeutic potential in combination with standard chemotherapy. Overall, this project aims to bridge systematic evidence synthesis with experimental validation to uncover novel post-chemotherapy metabolic vulnerabilities in childhood cancers, ultimately informing future therapeutic strategies to reduce relapse and improve clinical outcomes.

Supervision and Research Environment: The project will be supervised by Dr Kenny Yeo, an early-career researcher with expertise in both wet-lab and bioinformatics approaches, and experience mentoring Honours, Master's, and PhD students. Additional supervision and guidance will be provided by A/Prof Belamy Cheung and Prof. Glenn Marshall, both of whom bring extensive experience in paediatric cancer research at the Children's Cancer Institute. The student will be embedded within the Embryonal Cancer Therapy and Prevention Group, led by Prof. Marshall, a leading paediatric oncologist with a strong translational focus, ensuring the project remains clinically relevant and impact-driven.

PROJECT 2

Project Title: **Therapeutic Targeting of Chemo resistant Subclones Identified by Single-Cell Transcriptomic Profiling in Sarcomas**
Supervisor: Dr Parisa Vahidi Ferdowsi pvahidi@ccia.org.au
A/Prof Belamy Cheung bcheung@ccia.org.au
Suitable for: Honours, ILP or PhD Students

Project outline:
Most childhood, adolescent, and young adult (AYA) sarcoma patients achieve clinical remission through a "one-size-fits-all" chemotherapy regimen based on histological subtype. However, approximately one-third of these patients experience relapse, and the majority of those will ultimately die from the disease. This underscores an urgent need for accurate predictive assays to identify patients at risk of relapse.

Longitudinal studies have revealed the presence of minor sub clonal cancer populations at diagnosis that persist through early chemotherapy and later contribute to disease recurrence. The advent of single-cell RNA sequencing (scRNA-seq) has enabled high-resolution insight into the transcriptomic profiles of these rare subclones.

At Embryonal Cancer Therapy and Prevention Group at Children's Cancer Institute we have established a high-throughput droplet-based scRNA-seq platform to investigate intratumoral and intertumoral heterogeneity in osteosarcoma. Using proof of principle experiments on matched pre- and post-chemotherapy osteosarcoma samples, we identified an enrichment of chemo resistant subclones, some of which exhibit potential sensitivity to therapeutic agents not currently employed in standard treatment protocols. To further refine our ability to identify tailored therapies for osteosarcoma patients, we are expanding our capabilities to include single-nucleus RNA sequencing (snRNA-seq) and spatial transcriptomics (sRNA-seq).

Our study integrates cutting-edge scRNA-seq and whole-exome sequencing (WES) with advanced bioinformatics, large-scale public datasets, and unique clinical resources to address fundamental questions regarding the role of chemotherapy-resistant subclones in shaping individual patient outcomes.

Techniques and key outcomes /learnings:
The Higher Degree Research candidate will gain expertise in cutting-edge cellular and molecular techniques to investigate the hypothesis that changes in genomic and transcriptomic profiles among residual malignant cells during early chemotherapy reflect subclonal selection associated with chemoresistance and relapse.

Techniques and key outcomes /learnings:
- scRNA-seq, snRNA-seq, and sRNA-seq.
- Tissue culture
- Forward genetics using gene overexpression, knockdown and knockout.
- Cellular and molecular techniques including flow cytometry, RT-PCR and immunoblotting.
- Experience in working with patient-derived xenograft models of sarcoma.
- Data analysis and bioinformatics.
- Critical thinking and hypothesis testing.

PROJECT 3

Project Title: **A high-fat environment as a mechanism of initiation and progression of MYCN-driven medulloblastoma**

Supervisor: Dr Ritu Mittra sgadde@ccia.org.au
A/Prof Belamy Cheung bcheung@ccia.org.au

Suitable for: Honours or ILP Students

Project outline:
This Honours research project will investigate whether exposure to a high-fat environment accelerates medulloblastoma development, like findings recently observed in neuroblastoma models by our group. The project specifically focuses on the interaction between the MYCN oncogene, a known driver in both neuroblastoma and medulloblastoma, and a high-fat prenatal environment, mimicking maternal obesity. Medulloblastoma is the most common malignant paediatric brain tumour and a leading cause of cancer-related mortality in children. Relapsed medulloblastoma has extremely poor survival outcomes, underscoring the urgent need to understand the early drivers of disease. Our work in neuroblastoma showed that high-fat conditions in early development accelerates MYCN-driven oncogenesis. This project will test whether a similar mechanism exists in medulloblastoma using in vitro models.

The student will work primarily with medulloblastoma cell lines and compare the cellular and molecular responses of these cells in normal versus high-fat environments. Key analyses will include changes in proliferation, MYCN expression, lipid metabolism, and gene expression profiles indicative of tumour progression or transformation. If parallels are observed between neuroblastoma and medulloblastoma, this would support a broader paradigm of prenatal gene-environment interactions in embryonal tumour development.

Supervision and Research Environment: The project will be supervised by Dr Ritu Mittra, an experienced and dedicated researcher who has successfully co-supervised multiple HDR students with Associate Professor Belamy Cheung. Dr Mittra's last two Honours students were both awarded High Distinction, reflecting the high quality of mentorship and student support. The student will also be embedded within the laboratory of Professor Glenn Marshall at the Children's Cancer Institute. Prof Marshall is a leading paediatric oncologist with a strong translational focus, ensuring the research remains aligned with potential clinical impact.

Significance and Impact: Childhood cancer remains a major global health issue, with neuroblastoma and medulloblastoma accounting for a disproportionate number of cancer-related deaths in children. There is increasing evidence that gene-environment interactions in the prenatal period may contribute to cancer risk, yet the molecular mechanisms remain poorly understood. By exploring how a high-fat environment influences MYCN-driven medulloblastoma, this project addresses a critical knowledge gap. Understanding these mechanisms may lead to transformative strategies in early prevention, such as maternal dietary interventions, prenatal lipid screening, and the identification of epigenetic biomarkers of cancer risk. Given that maternal obesity affects over 30% of pregnancies globally, the potential to inform public health strategies and clinical interventions is substantial. This project could therefore yield findings of considerable scientific and societal importance, contributing to the broader goal of reducing childhood cancer incidence and improving outcomes for affected families.

FUNCTIONAL GENOMICS OF LEUKAEMIA GROUP

Group Leader: Associate Professor Charles De Bock

PROJECT 4

Project Title: **CRISPR activation screening to identify resistance mechanisms for a new AKR1C3-activated pro-drug in TCF3::HLF-positive leukaemia.**
Supervisor: Dr Hansen Kosasih hkosasih@ccia.org.au
A/Prof Charles De Bock cdebock@ccia.org.au
Suitable for: Honours
Project outline:
The clinical outcome of children diagnosed with TCF3::HLF positive B-cell acute lymphoblastic leukaemia (B-ALL) remains dismal and is essentially universally fatal. Currently there are limited treatment options with recent studies reporting relapses in patients undergoing immune therapies. Our research has demonstrated these cases are very sensitive to a new AKR1C3 activated pro-drug called ACHM-025.

This project will specifically aim to decipher mechanism of ACHM-025 resistance and sensitivity in TCF3::HLF-positive cell lines using a genome-wide CRISPR activation (CRISPRa) screening approach. The candidate genes will then be independently validated in follow up assays to determine how they drive resistance or increase sensitivity to ACHM-025. This knowledge will be critical for designing rational drug combination that can mitigate the development of resistance in the clinic.

Techniques the successful candidate will use and be trained in:
- Cell culture and lentiviral transduction of cell lines
- In vitro genome-wide CRISPR activation screening and bioinformatics analysis
- Cytotoxicity assay
- Molecular biology techniques including cloning, flow cytometry and immunoblotting

LEUKAEMIA BIOLOGY GROUP

Group Leader and Theme Head (Cancer Biology): Professor Richard Lock
Senior Research Officer: Dr Patrick Connerty
Senior Research Officer: Dr Narges Bayat

PROJECT 5

Project Title: **Developing novel targeted therapeutics for the treatment of paediatric acute lymphoblastic leukaemia**
Supervisor: Dr Sara Mohamed smohamed@ccia.org.au
Prof Richard Lock rlock@ccia.org.au
Suitable for: Honours, ILP or PhD Students
Project outline:
Philadelphia Chromosome like acute lymphoblastic leukaemia (Ph-like ALL) is a recently identified blood cancer with poor survival rates. These patients lack optimal treatment options and treatment with standard chemotherapy causes severe toxicity to healthy tissue. Targeted therapy is promising. However, the critical limitation of current targeted therapies against ALL is that they all target the same cell-surface proteins (antigens) on cancer cells. However, since these antigens are not functionally important, the cancer cells can escape treatment by removing them, thus becoming invisible to the therapeutic, leading to relapse. Moreover, these proteins are also expressed on both cancer and non-cancer cells, leading to side effects. There is an urgent need for new effective and safer targeted therapeutic approaches for the treatment of Ph-like ALL. We have addressed this challenge by targeting a cell-surface receptor

that is vital for the survival of the Ph-like ALL cells. In this project, students will develop novel therapeutics including antibody-drug conjugates (ADCs) against this target for the effective and safe treatment of Ph-like ALL.

Techniques and key outcomes/learnings:
- Site-specific conjugation of antibodies with chemotherapeutic drugs.
- Optimisation of the ADC properties including linker chemistry and antibody subtype.
- Cell and molecular techniques including cell cytotoxicity assays, flow cytometry, and confocal microscopy.
- Characterisation of the ADC including drug to antibody ratio.
- Experience in working with patient-derived xenograft models of ALL.

PROJECT 6

Project Title: **Evaluating novel therapeutics for treating paediatric acute myeloid leukaemia**
Supervisor: Dr Patrick Connerty pconnerty@ccia.org.au
Prof Richard Lock rlock@ccia.org.au
Suitable for: Honours, ILP or PhD Students
Project outline:
Acute myeloid leukaemia (AML) is an aggressive blood cancer in children with poor survival rates, particularly for patients who relapse or do not respond to initial treatment. Current therapies rely heavily on intensive chemotherapy, which can cause severe side effects and lead to long-term health complications. There is an urgent need to develop safer and more effective treatments that can overcome drug resistance and improve outcomes for children with AML.

This project aims to identify and evaluate new therapeutic strategies for AML by combining molecular biology approaches, such as CRISPR Cas9 knockout and overexpression, flow cytometry, and high throughput drug screening with preclinical drug testing in highly translational models. Students will investigate how specific genes influence drug sensitivity and resistance and assess the potential of new therapies that could be rapidly translated into clinical use for paediatric AML patients.

Techniques and key outcomes /learnings:
- Cas mediated gene overexpression, knockdown and knockout
- Genome-wide and small library CRISPR/Cas screening in vitro and in vivo
- Cell and molecular techniques including viral transduction, flow cytometry, RT-PCR, and immunoblotting
- High-throughput drug screening of patient-derived xenograft and patient AML cells.
- Experience in working with patient-derived xenograft models of AML

PROJECT 7

Project Title: **Investigating the role of long non-coding RNAs in paediatric acute myeloid leukaemia**
Supervisor: Dr Patrick Connerty pconnerty@ccia.org.au
Prof Richard Lock rlock@ccia.org.au
Suitable for: Honours, ILP or PhD Students
Project outline:
Acute myeloid leukaemia (AML) is an aggressive blood cancer currently treated with intensive chemotherapy that kills both cancer and healthy blood cells leading to severe side effects and long-term health complications. 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 while sparing healthy blood cells. In this project, students will identify and investigate lncRNAs that are both specific and vital for AML cells and explore their potential as therapeutic targets.

Techniques and key outcomes/learnings:
- Forward genetics using siRNA, shRNA, CAS13 knockdown and Cas9 knockout
- Genome-wide and small library CRISPR/Cas screening in vitro and in vivo
- Cell and molecular techniques including viral transduction, flow cytometry, RT-PCR and immunoblotting
- Experience in bioinformatics analysis
- Experience in working with patient-derived xenograft models of AML

TRANSLATIONAL TUMOUR BIOLOGY GROUP

Group Leader and Deputy Director (Research Themes): A/Professor Paul Ekert
Senior Scientist: Dr Emmy Dolman

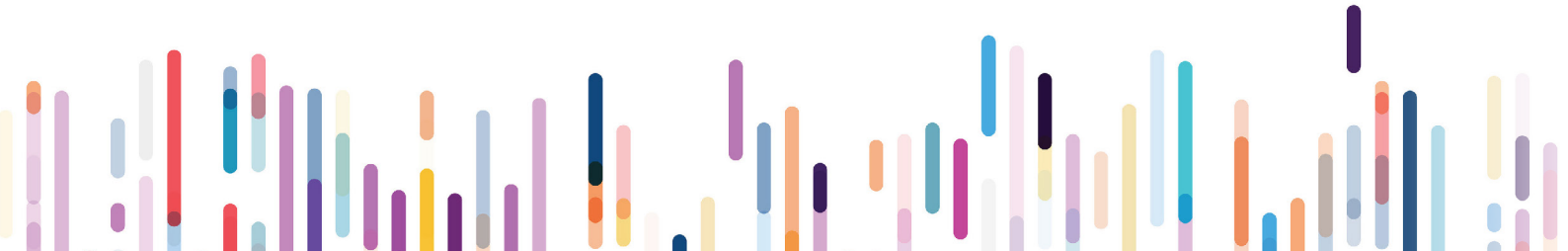
PROJECT 8

Project Title: **Integrative data analysis: from novel biomarker-drug response associations to predicting effective drug combinations**
Supervisor: Dr Emmy Dolman EDolman@ccia.org.au
Jie Mao jmao@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 9

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
Dr Gabor Tax
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.



PROJECT 10

Project Title: **The Functional Genomics of Molecular Targets in Paediatric Cancer**
Supervisor: Dr Pei Liu PLiu@ccia.org.au
A/Prof Paul Ekert pekert@ccia.org.au
Suitable for: Honours or PhD Student
Project outline:
Background: Cancer remains one of the deadliest diseases in children. Our Computational Drug Discovery Biology group and Translational Tumour Biology group work together on discovering novel gene targets for drug development in childhood cancers. This work leverages the remarkable genomic data available through the Zero Childhood Cancer Program (ZERO), the national precision medicine program for childhood cancer. The goal of this Honours/PhD project is to discover and experimentally validate molecular targets for drug discovery using the advanced tools of functional genomics, molecular and cellular biology.

Broadly, the research goals are to establish how selected molecular targets regulate cell survival and proliferation in paediatric cancer cells. The experimental approaches include gene-knockout or knockdown system such as the RNA-guided Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) Cas9 and Cas13d. The assays that are used to read out the effects of gene perturbation include RT-PCR, western blotting, cell cytotoxicity, cell proliferation and clonogenicity assays. It may also include RNA-sequencing and quantitative proteomics analyses. Once it is established that a target has potential, the student will undertake further detailed molecular analyses to demonstrate in detail the molecular functions of the target gene in cancer cells, which enzymatic or other functions of the molecule are required for any oncogenic activity and what the consequences would be of disrupting those functions.

The student will have the opportunity to be involved in the development of assays to screen for possible small molecules to that could form the basis of future drug development. The student will develop skills in advanced skills in molecular biology and functional genomics. The student will also develop skills in computational biology and bioinformatics. They will work as part of the Translational Tumour Biology and Computational Drug Discovery groups. This is an ideal project for a student curious about the fundamental biological processes that drive the cancer phenotype, and a desire to learn how basic science can drive therapeutic discoveries.

PROJECT 11

Project Title: **Genome-wide CRISPR Screening to Identify Dependencies in High-Risk Paediatric Cancer**
Supervisor: Dr Hansen Kosasih hkosasih@ccia.org.au
A/Prof Paul Ekert pekert@ccia.org.au
Suitable for: Honours or PhD Student
Project outline:
Despite major advances in the treatment of childhood cancer, many children with high-risk malignancies continue to experience poor outcomes or relapse following intensive therapy. Our research aims to identify the genetic dependencies in these aggressive cancers as a key pathway to identifying more effective and less toxic targeted treatments aimed specifically at the vulnerabilities of the cancer. At the same time, we seek to understand how the molecular changes that arise in childhood cancers drive the acquisition of the hallmarks of malignant cells, in particular unrestricted cell proliferation and resistance to cell death.

This project will utilise resources including cell lines and data from the ZERO Childhood Cancer precision medicine program, Australia's national initiative for comprehensive molecular profiling of childhood cancers. We will use cutting-edge functional genomics approaches including genome-wide CRISPR/Cas9 loss-of-function screens to systematically identify genetic dependencies across high-risk paediatric cancer cell lines. Candidate genes emerging from these screens will be prioritised for validation through mechanistic studies to determine how these genes contribute to tumour cell survival and proliferation.

Techniques the successful candidate will use and be trained in:
- Cell culture and lentiviral transduction of cell lines
- In vitro genome-wide CRISPR/Cas9 knock-out screening
- Other CRISPR based methodologies (CRISPR base editors)
- Molecular biology techniques including cloning, flow cytometry and immunoblotting
- Epigenetics techniques including ATAC-Seq, ChIP-Seq, and HiChIP

COMPUTATIONAL BIOLOGY GROUP

Group Leader & Deputy Director (Enabling Platforms + Collaboration): A/Professor Mark Cowley

PROJECT 12

Project Title: **The onco-mitochondrial landscape of childhood cancer**
Supervisor: Dr Piyushkumar Mundra PMundra@ccia.org.au
A/Prof Mark Cowley mcowley@ccia.org.au
Suitable for: PhD Students
Project outline:
Mitochondria play a critical role in cellular energy production and various metabolic functions. Compared to nuclear genome in humans (~3.3 billion base pairs), the mitochondrial genome is a small, circular DNA molecule comprising 16,569 base pairs, encoding essential genes, transfer RNAs (tRNAs), and ribosomal RNAs (rRNAs). Each mitochondrion harbors multiple copies of mitochondrial DNA (mtDNA), and a single cell can contain hundreds to thousands of mitochondria—resulting in several thousand copies of the mitochondrial genome per cell. Pathogenic variants in mtDNA can occur in all copies (homoplasmy) or in only a subset (heteroplasmy). Numerous studies have linked mtDNA alterations to tumorigenesis in adult cancers. However, genomes of paediatric cancers are very different from adult cancers with different cell of origin. Hence understanding role of mtDNA alterations in pan-paediatric cohort is an important research question that remains unexplored till date.

Leveraging samples from Australia's largest paediatric precision oncology initiative—the ZERO Childhood Cancer Program—we have performed whole-genome sequencing on over 2,000 tumour-normal paired samples. For this project, our first aim is to create a comprehensive landscape of mtDNA-specific somatic and germline alterations across various paediatric cancers. Our laboratory has developed a bioinformatics pipeline, mity, to detect germline mtDNA variants. We plan to expand this pipeline to incorporate somatic mutations, as well as mtDNA copy number and structural variants.
In addition to genomic data, we have access to extensive clinical and molecular datasets from ZERO participants, including pathogenic and likely pathogenic alterations in the nuclear genome, as well as RNA expression and methylation profiles. We will aim to perform integrative enrichment analyses comparing tumours with and without mtDNA alterations. Furthermore, with data from over 100 patients with multiple tumour samples, we aim to study the evolutionary dynamics of mtDNA alterations over time and in response to therapeutic interventions.

To further enhance our resolution of mitochondrial genomic variation, we will employ long-read sequencing technologies such as Oxford Nanopore. These technologies produce reads spanning several kilobases, allowing the entire mitochondrial genome to be sequenced in a single or few reads. This approach will improve the accuracy of variant detection, especially in regions with high homopolymer content. We plan to sequence tumour samples from a range of paediatric cancer types using this method, generating a unique dataset that will support the development of novel computational tools for identifying somatic mtDNA alterations.

The PhD candidate will be based in the Computational Biology Laboratory at the Children's Cancer Institute, Sydney. They will benefit from access to world-class computational infrastructure, unique datasets, and strong interdisciplinary support from a team of experienced researchers and engineers.

PROJECT 13

Project Title: **Transcriptomic analysis of locus specific LINE-1 activity in paediatric cancer**
Supervisor: Dr Nandan Deshpande NDeshpande@ccia.org.au
Suitable for: Honours Students
Project outline:
Approximately half of the human genome consists of transposable elements (transposons), mobile DNA sequences that have, or once had, the ability to move within the genome. These elements are increasingly recognised as contributors to cancer development and progression through the disruption of functionally important genes.
This project will use transcriptomic (RNA-seq) data from paediatric tumours to investigate the activity of Long Interspersed Nuclear Element-1 (LINE-1), the only autonomously active transposable element family in the human genome. Although highly repetitive genomic regions are difficult to analyse using conventional short-read RNA-seq data, recently developed bioinformatics tools employing expectation-maximisation algorithms enable locus-specific quantification of LINE-1 expression. The Honours student will apply these tools to a cohort of paediatric cancer samples to identify, quantify, and characterise locus-specific LINE-1 activity and evaluate its impact on the tumour

transcriptome. Downstream analyses will investigate heterogeneity in LINE-1 expression, identify recurrent or highly active loci, assess patterns across the cohort, and explore associations between LINE-1 activity and molecular or clinical features, including measures of genomic instability.
A pilot set of long-read RNA-seq data is expected to become available during the project, providing an opportunity to compare and validate findings derived from short-read sequencing. In future studies, these results could be integrated with whole-genome sequencing (WGS) and DNA methylation data to generate a comprehensive multi-omics landscape of somatic LINE-1 activity. Such analyses can help elucidate relationships between LINE-1 transcription, somatic retrotransposition, novel LINE-1 insertions, genomic instability, and tumour evolution. Improved understanding of these processes may provide insights into mechanisms underlying tumour progression and relapse, a major challenge in the treatment of paediatric cancer.

This project will generate one of the first locus-specific maps of LINE-1 transcriptional activity in a paediatric cancer cohort and provide new insights into how transposable element activity contributes to tumour biology and genomic instability. The student will gain hands-on experience in cancer genomics and computational biology, including RNA-seq analysis, high-performance computing, bioinformatics workflow development, statistical analysis, data visualisation, and integration of genomic and clinical datasets. The student will gain hands-on experience in cancer genomics and computational biology, including RNA-seq data analysis, high-performance computing, bioinformatics workflow development, statistical analysis, data visualisation, and the integration of genomic and clinical datasets.

SARCOMA BIOLOGY AND THERAPEUTICS GROUP

Team Leader: A/Prof Emmy Fleuren

PROJECT 14

Project Title: **Discovering actionable drug targets for young patients with sarcoma through phosphoproteomics**
Supervisor: A/Prof Emmy Fleuren efleuren@ccia.org.au
Suitable for: Honours, ILP or PhD Students
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.

PROJECT 15

Project Title: **Finding better and kinder treatments for young patients with osteosarcoma and beyond**
Supervisor: A/Prof Emmy Fleuren efleuren@ccia.org.au
Suitable for: Honours, ILP or PhD Students
Project outline:
There is an unmet need to identify better and kinder treatments for young people with osteosarcoma. Osteosarcoma

is an aggressive and difficult-to-treat type of cancer that disproportionally affects the young. Treatments have not changed much over the past four decades, and still consist of surgery (often amputation), high dose chemotherapy and sometimes radiotherapy. Side-effects are frequent, and despite this intense treatment, still not everyone makes it. The expected chance of survival is less than 20% when the tumour is metastasized, which is not uncommon at diagnosis.

We recently established 8 unique patient-derived osteosarcoma cell models, and by testing a range of novel drugs on these cells, found a promising new drug to treat osteosarcoma. While this drug was on its own already stopping the growth of osteosarcoma cells grown in a dish in the lab ('in vitro'), and even stopped the growth of real mini human osteosarcoma tumours grown in mouse avatars ('in vivo'), a combination of this drug with another targeted drug was even more effective and very tolerable. Excitingly, our latest data suggests this combination may also work for other aggressive sarcomas, thereby vastly extending the impact of our work. In some instances, we even observed complete tumour regressions.

Now, more work is needed to truly pinpoint who is most likely to benefit from this novel (combination) treatment. We need to 1) understand why and how these drugs work, and 2) test our drugs in more sarcoma avatar models, which represent the 'gold standard' of drug testing. This is the type of evidence we need to generate to make new drugs a treatment reality for 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 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 research techniques, such as phosphoproteomics, Western Blot, functional knock-out/down (e.g. CRISPR/siRNA), immunohistochemistry, in vitro drug assays, and when applicable in vivo studies. Exact techniques depend on Honours/PhD level.

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

BRAIN TUMOURS GROUP

Group Leader: Professor David Ziegler
Senior Scientist: Associate Professor Maria Tsoli
Senior Scientist: Dr Ben Rayner

PROJECT 16

Project Title: **Exposing the enemy: epigenetic therapy reveals hidden viral passengers with oncogenic potential in DIPG**
Supervisor: Dr Benjamin Rayner brayner@ccia.org.au
Prof David Ziegler d.ziegler@unsw.edu.au
Suitable for: Honours or ILP Students
Project outline:
Approximately 12% of all human cancers are caused by viral infection. These 'oncoviruses' trigger hallmark alterations that underlie the tumour's malignant characteristics, including mutations that switch on multiple genes that lead to uncontrolled growth, genetic instability, immune evasion and cancer cell survival. Notably, these factors mirror the landscape of DIPG – the most aggressive and incurable cancer of childhood. These tumours have specific genetic changes that occur for unknown reasons, leading to abnormal control of genes switching on and off, in turn leading to uncontrolled tumour growth. They also create an environment that weakens the body's immune response to the tumour.

To date a direct link between oncoviruses and DIPG tumour development has yet to be proven. This may be due to the ability of many viruses to enter a dormant stage, remaining effectively hidden within the tumour's genetic code. Excitingly, we have shown that treatments that alter the way that DNA is packaged and read are able to reveal previously undetected oncogenic viruses within DIPG. We hypothesize that by exposing these viral constituents in this manner allows for the targeting of them with antiviral therapies, leading to the eradication of these potential DIPG drivers, subsequently terminating DIPG growth.

PROJECT 17

Project Title: **Discovery and evaluation of novel targeted drug combinations for aggressive paediatric ependymoma**
Supervisor: A/Prof Maria Tsoli mtsoli@ccia.org.au
Dr Yongjuan (Joan) Chen ychen@ccia.org.au

Suitable for: Honours or ILP Students
Project outline:
Intracranial ependymomas (EPNs) are aggressive brain tumours, accounting for approximately 30% of brain tumours in children younger than 5 years old. Two subtypes of EPNs, supratentorial EPN (ST-EPN) and posterior fossa group A ependymoma (PFA-EPN), are the most aggressive and are each with specific molecular alterations. Approximately 70% of ST-EPNs are harbouring with an oncogenic ZFTA–RELA gene fusion. And PFA-EPNs are characterised by epigenetic modifications with EZHIP overexpression and H3K27me3 loss. The gene alterations in ST-EPNs and PFA-EPNs could be the promising therapeutic vulnerabilities. So far, no effective targeted therapy currently exists for paediatric EPNs.

In our group, we have successfully established patient-derived xenograft (PDX) mouse models. We have also demonstrated the synergistic cytotoxic effects of combining two drugs that target specific molecular vulnerabilities in EPN cells. These combinations also induce apoptosis and downregulate key survival proteins, indicating their potential as therapeutic candidates for EPN.

The aims of this project are to:
- Evaluate the therapeutic efficacy of targeted drug combinations and drugs-irradiation combinations across a panel of ST-EPN and PFA-EPN cell lines in vitro.
- Elucidate the underlying mechanisms of action driving the synergistic effects in EPN cells.

You will carry out the experiments on:
- Drug screening by using cytotoxicity assay and clonogenic assay.
- Mechanism of action of drug combinations by using qPCR, Western blotting, immunofluorescence, and flow cytometry

By the end of this project, you will achieve robust evidence for the therapeutic effects of novel drug combinations in paediatric EPN cells and identify the molecular pathways with the combined treatments, supporting future in vivo studies and clinical translation.

PROJECT 18

Project Title: **Developing therapies to overcome the high-lactic acid tumor environment induced in DMG**
Supervisor: Dr Jessica Bell jbell@ccia.org.au
Prof David Ziegler d.ziegler@unsw.edu.au
Suitable for: PhD, Honours or ILP Students
Project outline:
Most tumors have a cloud of lactic acid around them promoting tumour growth but also preventing lasting activity and penetration of anti-cancer immune cells. In adult cancer models, scientists have demonstrated that when drugs are used to reduce the lactic acid, the tumor cells grow slower and the anti-tumour, immune responses are improved. Children's brain tumors also have elevated levels of lactic acid compared to the surrounding healthy brain. It remains unknown if lactic-acid lower drugs might offer benefit against children's brain tumors (such as deadly DMG).

The project investigates therapies to overcome the high-lactic acid tumor environment induced in DMG. Students will learn how to test different drug combinations, perform live cell microscopy, metabolism biochemical assays and other techniques.

There are various project options (focusing on proteomics, immune response or epigenetic changes) and we can create a project that suits both the supervisory team and students interests.

CANCER TARGETS AND THERAPEUTICS GROUP
Research Fellow: Dr Angelica Merlot

PROJECT 19

Project Title: **Specific Targeting of Tumour-Promoting Cancer-Associated Fibroblasts in Pancreatic Cancer**
Supervisor: Dr Angelica Merlot AMerlot@ccia.org.au
Prof Minoti Apte m.apte@unsw.edu.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.

PROJECT 20

Project Title: **Examining the Surfaceome of Brain Cancer Cells to develop novel therapeutics**
Supervisor: Dr Angelica Merlot AMerlot@ccia.org.au
A/Prof Tushar Kumeria t.kumeria@unsw.edu.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.

PROJECT 21

Project Title: **Targeting polyamines to eradicate the root of relapse in neuroblastoma**
Supervisor: Dr Angelica Merlot AMerlot@ccia.org.au
Dr Klaartje Somers ksomers@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.

CHEMICAL BIOLOGY AND TARGET BASED THERAPIES GROUP

Team Leader: Dr Jean Bertoldo

PROJECT 22

Project Title: **Integrating data science, chemical biology, and basic biology to uncover the AML druggable proteome with small-molecule covalent ligands**
Supervisor: Dr Jean Bertoldo jbertoldo@ccia.org.au
Suitable for: Honours or PhD Students
Project outline:
Acute myeloid leukaemia (AML) is an aggressive childhood cancer with high unmet need and poor survival rates. Alternative therapies, such as targeted small molecules, need to be developed as current chemotherapies result in severe side effects and long-term health complications. Our group has previously identified targets for solid paediatric

cancers and paired them with small-molecule covalent ligands that are now progressing through the drug discovery pipeline. Preliminary analysis suggests AML is comparatively rich in dependencies, offering many avenues to explore covalent therapeutic options in this disease.

This study aims to identify targets AML relies on, that normal cells do not need, and further develop covalent ligands targeting these dependencies. This project encompasses data science and basic biology – to identify and validate dependencies within AML – as well as chemical biology – to develop covalent ligands into drug-like molecules against these novel targets.

Techniques and key outcomes/learnings:
- Data mining to identify and validate targetable dependencies in AML (computational).
- Cell line screening assays to prioritise covalent ligands with selective anti-cancer activity (IC50 assays).
- On-target engagement of covalent ligands to intended targets (CETSA/DARTS).
- Proteomics/RNA-sequencing to uncover biological pathways and mechanistic insights into how covalent ligands work (Mass spectrometry/RNA-seq/cell-based assays).

About the group:
Our group designs new small-molecule therapeutics for various cancers by combining many fields of science including biology, chemistry, and data science. The projects within the group aim to carry discoveries forward through the drug discovery pipeline to develop safer, more targeted therapies.

PROJECT 23

Project Title: **Development of covalent ligand inhibitors for IGF2BP3**
Supervisor: Dr Jean Bertoldo jbertoldo@ccia.org.au
Suitable for: PhD Students
Project outline:
IGF2BP3 is an RNA-binding protein implicated in multiple cancers including neuroblastoma, an aggressive childhood cancer. We have previously employed an in-house drug discovery pipeline to identify small-molecule covalent ligand CL174 that binds IGF2BP3, which, despite various efforts, has not previously been successfully drugged.

CL174 has already demonstrated anti-cancer activity, a strong selectivity window compared to normal human cells, on-target engagement, and functional modulation of IGF2BP3. However, medicinal chemistry efforts still need to be employed to further optimise CL174 into a drug-like molecule before testing in vivo. This multi-field project encompasses chemistry, chemical biology, and basic biology with the aim of developing CL174 into a drug-like molecule for the treatment of neuroblastoma.

Techniques and key outcomes/learnings:
- Medicinal-chemistry design and structure-activity relationship (SAR) analysis.
- Synthesis of covalent-ligand analogues.
- Biochemical and cell-based potency and selectivity assays.
- In vivo pharmacokinetic/pharmacodynamic studies of a lead compound.

About the group:
Our group designs new small-molecule therapeutics for various cancers by combining many fields of science including biology, chemistry, and data science. The projects within the group aim to carry discoveries forward through the drug discovery pipeline to develop safer, more targeted therapies.

PROJECT 24

Project Title: **Development of covalent ligands as inhibitors of IPO4 for multiple cancers**
Supervisor: Dr Jean Bertoldo jbertoldo@ccia.org.au
Suitable for: Honours or PhD Students
Project outline:
Importin-4 (IPO4) plays a crucial role in nuclear import, and has been previously linked to glioblastoma. Our in-house drug discovery pipeline has identified IPO4 as a dependency in glioblastoma, but also lung adenocarcinoma and oral cavity squamous cell carcinoma. This project evaluates whether IPO4 is a genuine, broadly relevant and druggable target in all three cancers. In this study, small-molecule covalent ligands will be screened to test on-target engagement, anti-cancer activity, and functional modulation with the aim of progressing a covalent ligand into a small-molecule therapeutic targeting IPO4.

Techniques and key outcomes/learnings:
- Mining dependency and expression datasets to validate IPO4 as a dependency in glioblastoma, lung cancer, and oral cavity squamous cell carcinoma (Computation)
- Cancer cell culture and gene silencing (siRNA)
- Cytotoxicity and selectivity assays (IC50/colony formation)
- Target-engagement testing of candidate covalent ligands (CETSA/DARTS)
- Mechanistic insights (cell-based assays, western blots).

About the group:
Our group designs new small-molecule therapeutics for various cancers by combining many fields of science including biology, chemistry, and data science. The projects within the group aim to carry discoveries forward through the drug discovery pipeline to develop safer, more targeted therapies.

COMPUTATIONALLY ENABLED DRUG DISCOVERY GROUP / THINK

Group Leader: A/Professor Antoine de Weck

PROJECT 25

Project Title: **Functional validation of engineered U1 snRNAs targeting cancer-relevant poison exons**
Supervisor: A/Prof Antoine de Weck adeweck@ccia.org.au
Dr Pragya Gupta pgupta@ccia.org.au
Dr Pablo Aceras Mateos PAceraMateos@ccia.org.au
Suitable for: Honours or ILP Students
Project outline:
Cancer cells often exploit changes in RNA processing to support uncontrolled growth, survival and treatment resistance. One important but underexplored layer of gene regulation is pre-mRNA splicing, the process by which non-coding introns are removed, and coding exons are joined to produce mature messenger RNA. Some transcripts contain poison exons, which introduce premature stop signals and can reduce productive gene expression. Learning how to control poison-exon inclusion could provide new tools to study cancer-associated genes and uncover vulnerabilities in aggressive cancers.

Our team is developing engineered versions of U1 small nuclear RNA, a core spliceosomal RNA that recognises 5′ splice sites on pre-mRNAs. These engineered U1s are designed to redirect splice-site recognition at selected poison exons in cancer-relevant transcripts. Before these tools can be used in larger functional screens, we need to validate whether engineered U1 expression produces measurable, target-specific changes in transcript output. We will also use SHAPE-MaP, a sequencing-based RNA structure probing method, to examine whether engineered sequence alters the folding and structural accessibility of variant U1 snRNAs.

Techniques and key outcomes/learnings:
- Mammalian cell culture and plasmid transfection of engineered U1 snRNA constructs.
- Fluorescence microscopy and/or flow cytometry to assess construct delivery and transfection efficiency.
- RNA extraction, cDNA synthesis, primer designing and targeted RT-qPCR analysis of transcript abundance.
- Establishment of SHAPE-MaP workflow steps, including RNA chemical modification, reverse transcription, library preparation optimisation and next generation sequencing-readout assessment.
- Experience in RNA biology, pre-mRNA splicing, engineered snRNA design and molecular assay development.

PROJECT 26

Project Title: **Automating biology to accelerate AI-guided drug discovery**
Supervisor: A/Prof Antoine de Weck adeweck@ccia.org.au
AJ Sethi ASethi@ccia.org.au
Suitable for: Honours or ILP Students
Project outline:
STUDENT WANTED
for hazardous journey, small wages, bitter cold, long months of complete darkness, constant danger, safe return doubtful...

A fundamental challenge: measuring complex systems at industrial scale.

- From basic science to precision drug development, a central challenge in biotechnology is understanding how perturbations (e.g. drug treatments, genetic manipulation, or environmental changes) impact dynamic systems

(e.g. cells, tissues, organs), using high-dimensional, mechanistically informative, quantitative readouts (e.g. gene expression assays, high-content imaging, -omics technologies, etc).
- While academic research has benefitted from incredibly powerful measurement technologies, in general, the cost, complexity, and lack of scalability of these assays is a fundamental bottleneck that prevents or constrains routine data acquisition across thousands or millions of perturbations.
- In our context – the development of novel therapeutics for childhood cancers – limitations on the rate at which we can acquire new types of data are one of the fundamental bottlenecks in our preclinical drug development campaigns.
- The data bottleneck affects the rate at which targets can be identified, new compounds tested, and predictions generated and creates an urgent unmet need that will be the basis of your Honours project.

The mission: development of solutions for industrial-scale biological measurement

- We are developing end-to-end systems to measure rapid cellular responses to pharmacological perturbation at scale. When successful, the data we acquire will accelerate our drug development campaigns – and if achieving scalability targets – could be a valuable source of training data for Bio x AI models.

The journey:

- You will join us as a full-stack trainee who develops experience across our entire process development and takes intellectual ownership of one slice of our technical workflow.
- Your project will be developed in response to your skills, interests, capabilities and ambitions; We are open to training motivated students with experience in any relevant fields (including, but not limited to, bio/chem/med.sci/eng/comp.sci backgrounds)
- You'll develop the ability to perform interdisciplinary reasoning across chemistry, biology, hardware and code — with experience across all of these fields and technical expertise across your specifically-chosen domain.
- You will be challenged. The work will be difficult, the timelines will be tight, the learning curve will be steep, and the problems you are genuinely unsolved with significant global competition.
- The solutions you help to build could have real world impact on how we measure biological systems and acquire data to solve fundamental challenges in science and medicine.

...Honours and recognition in case of success.

PROJECT 27

Project Title: **Reactivation of Tumour Suppressor Genes via RNA Splicing Engineering**
Supervisor: Dr Sasanan Trakansuebkul strakansuebkul@ccia.org.au
A/Prof Antoine de Weck adeweck@ccia.org.au
Suitable for: Honours Students
Project outline:
Cancer Tumour suppressor genes (TSGs), including TP53, PTEN, and RB1, play a critical role in preventing uncontrolled cell growth. In many cancers, these genes are inactivated by mutations that disrupt RNA splicing, the process by which non-coding regions (introns) are removed and coding regions (exons) are joined to form functional messenger RNA (mRNA).

Splicing is guided by short sequence elements such as the 5′ splice site. Mutations affecting these sites can lead to incorrect splicing, resulting in truncated or non-functional proteins and loss of tumour suppressor activity. This project aims to restore TSG function by correcting splicing defects at the RNA level using engineered U1 small nuclear RNA (U1 snRNA), a key component of the spliceosome. Modified U1 molecules can be designed to recognise mutated splice sites and promote correct exon inclusion.

A central focus of the project is to understand how local sequence context, including nearby "cryptic" splice sites (alternative splice signals), influences splicing outcomes. In some cases, these nearby sites compete with the intended splice site, leading to aberrant transcripts that may not restore gene function.

To systematically study these effects, the project will use minigene constructs, which are simplified gene models containing selected exons and introns. These allow controlled investigation of splicing behaviour in human cells. This project addresses a key challenge in RNA therapeutics: determining when splicing correction can successfully restore functional tumour suppressor activity.

Findings will improve our understanding of splice-site selection and context-dependent regulation, and help identify

which mutations are suitable targets for RNA-based therapies. This work has potential to inform future therapeutic strategies aimed at reactivating tumour suppressor genes in cancer.

Techniques and key outcomes
- Molecular cloning and minigene design
- Mammalian cell culture and transfection
- RNA extraction and RT-PCR
- Amplicon-based RNA sequencing and data interpretation
- Understanding of RNA splicing mechanisms and therapeutic targeting strategies

EXPERIMENTAL THERAPEUTICS & MOLECULAR ONCOLOGY GROUP

Group Leaders: Professor Michelle Haber and Professor Murray Norris
Principal Scientist + A/Professor: Jamie Fletcher

The aim of the Experimental Therapeutics Group is to develop more effective, targeted treatments for childhood solid tumours, with a particular focus on 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.

PROJECT 28

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 29

Project Title: **Novel combination therapies for child, adolescent and young adult sarcoma**
Supervisor: Prof Michelle Haber MHaber@ccia.unsw.edu.au
Prof Murray Norris MNorris@ccia.org.au
A/Prof Jamie Fletcher jfletcher@ccia.org.au
Dr Jayne Murray jmurray@ccia.org.au
Suitable for: Honours or PhD Students
Project outline:
We have developed a series of novel therapies targeting child cancer driver signals in sarcoma: polyamine metabolism using DFMO/AMXT1501; chromatin conformation using FACT inhibitor CBL0137; nicotinamide metabolism with inhibitor OT-82; arginine dependency using pegylated arginase BCT-100. We use unbiased high-throughput

combination to identify synergy with established oncology drugs. Effective combinations will be validated in vivo in our internationally unique panel sarcoma PDX models. For biomarker identification, PDX response scores will be integrated with RNA seq and genomic datasets from sarcoma patients to identify differentially expressed genes, enriched pathways and molecular aberrations in responders.

TRANSLATIONAL CANCER NANOMEDICINE GROUP

Group Leader: Professor Maria Kavallaris
Senior Scientist: Dr Anna Guller
Senior Research Officer: Dr Ernest Moles Meler

PROJECT 30

Project Title: **Engineering childhood cancer models for precision medicine**
Supervisor: Prof Maria Kavallaris mkavallaris@ccia.org.au
Dr Anna Guller aguller@ccia.org.au
Suitable for: Honours, ILP 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 31

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
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.

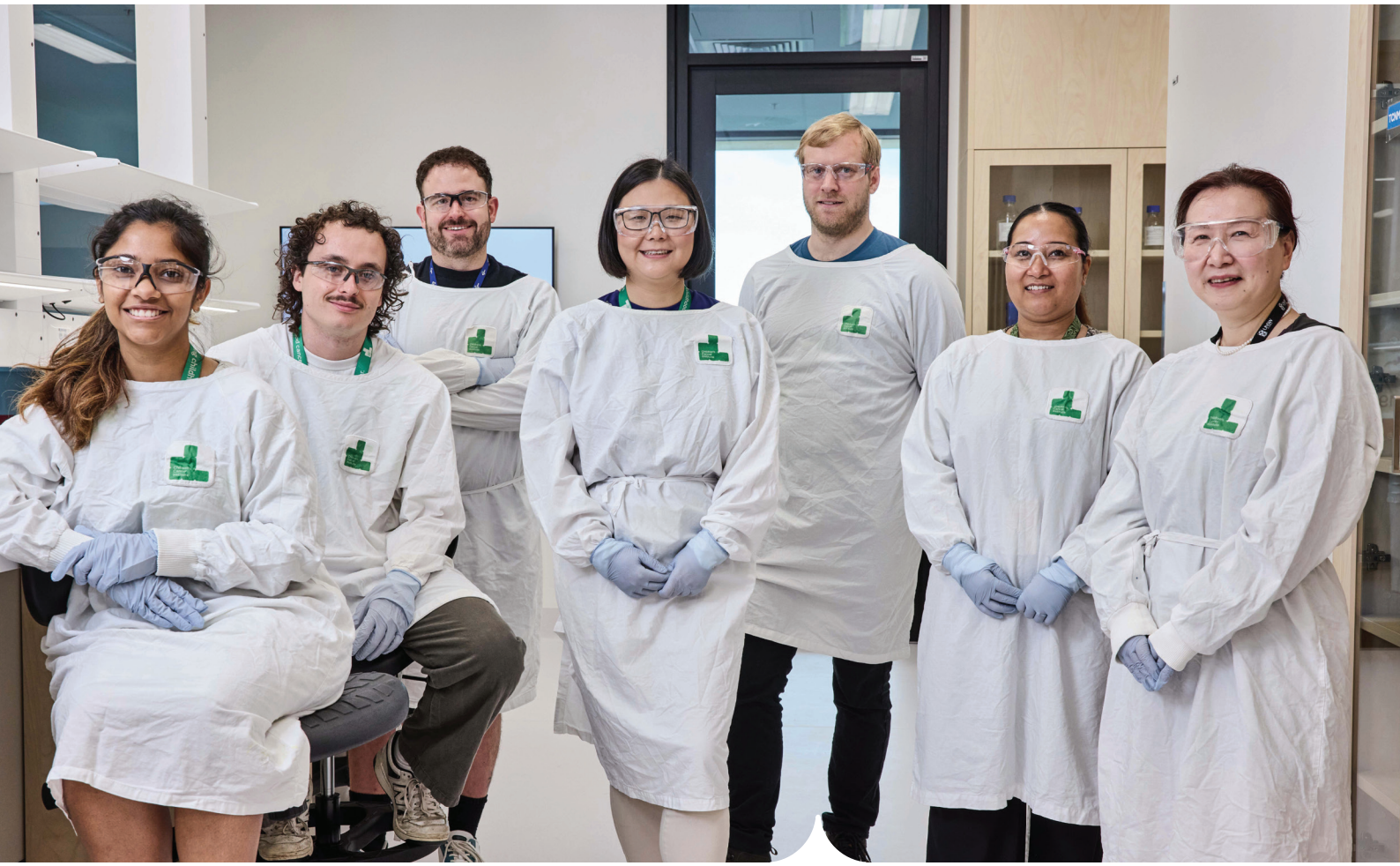
PROJECT 32

Project Title: **Engineering Precision RNA Therapies for Childhood Cancer**
Supervisor: Prof Maria Kavallaris mkavallaris@ccia.org.au
Dr Amy Logan alogan@ccia.org.au
Suitable for: PhD Students
Project outline:
Despite significant advances in cancer treatment, many children with aggressive or drug-resistant cancers continue to face poor outcomes, while survivors often experience lifelong treatment-related side effects. New therapeutic approaches are urgently needed that are more effective, less toxic and tailored to the biology of each patient's tumour.

This PhD project will investigate novel precision therapies for high-risk childhood cancers by combining cancer biology, functional genomics, RNA therapeutics, nanomedicine and bioengineering. The research will focus on identifying critical molecular dependencies that drive tumour growth, survival and treatment resistance, and developing innovative strategies to target these vulnerabilities.

The project will address three key questions: Which genes and pathways are essential for cancer cell survival? How can these vulnerabilities be exploited using RNA-based therapeutics to maximise anti-tumour activity while minimising toxicity? And how can delivery systems be engineered to ensure therapies reach tumours efficiently and overcome treatment resistance?

Using cutting-edge technologies, including CRISPR screening, RNA interference, patient-derived cancer models, 3D bioprinted tumouroids, advanced imaging and nanoparticle-based drug delivery, the student will help develop next-generation precision medicines. This interdisciplinary project offers training at the interface of cancer research, genomics, nanotechnology and translational medicine, with the ultimate goal of delivering more effective and personalised treatments for children with cancer.



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 **www.ccia.org.au** for more information.

Children's Cancer Institute

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Children's Cancer Institute

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