CHILDREN'S LEUKAEMIA + CANCER RESEARCH FOUNDATION

Annual Report 2020-21

Children's Leukaemia & Cancer Research Foundation (Inc.)

Funding research into childhood cancers for over forty years

Contents

A message from The Foundation

Thank you to the wonderful people and businesses who supported the Foundation during another challenging year. Due to that support, the Foundation is still going strong and growing its research potential for our children's future.

The current economic downturn has presented the Foundation with a deficit of $63,984 before research funding. It was an expected outcome as we had embarked on our Growth Strategy early in 2021. To support our internal capabilities to achieve the growth we need, we appointed a Donor Fundraising Specialist and a Marketing Manager.

Due to the fact the Foundation has been able to keep accumulated funds in reserve for research expenditure, all research commitments of $1,063,297 were met, leaving a total deficit of $1,127,281.

It should be mentioned that since the very first dollar was donated to CLCRF, over $35.9M has been raised for childhood cancer research. That is something this Foundation and those associated with its legacy feel very proud of achieving.

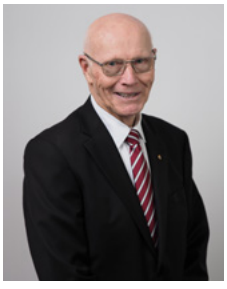
The Foundation has also just committed to funding $3,299,460 in research grants for the next three years. It is hoped in the future that the Foundation can provide support to cancer children and their families as well as the continued childhood cancer research.

The year 2021 was a year of "celebrating 'relationships". We are thankful for the continued cooperative working relationship we enjoy with the Telethon Kids Institute and extend appreciation to Professor Jonathan Carapetis AM, the Institute's Director and Ms Julie Bishop, the Institute's Chairperson. The dedication of all the researchers and their teams who undertake the vital life-saving work into childhood cancers must also be noted.

The past 12 months have not been kind to our cancer families with the loss of many children to this horrible disease. Our heartfelt sympathy goes out to each one of those families. The Foundation was originally formed by families who had a child diagnosed with cancer, to fund research so that no family lost their child to this disease. The children were given the chance to defeat this cancer and, to hopefully, go on to live normal lives. That is still our objective today.

We could not continue this critical work without the support of people, and the Foundation continues to be humbled by the generosity of the WA community in assisting with our mission.

We look forward to the year ahead to ensure childhood cancer research in WA is world-class. Furthermore, it ensures that our children are getting the best care and treatments possible.



Mr Geoffrey Cattach, AM
CHAIRMAN

Mrs Andrea Alexander
CHIEF EXECUTIVE OFFICER

Committee of Management

AS AT 30/06/2021

Mr Geoffrey Cattach, AM
CHAIRMAN

Mr Philip Bruce
VICE CHAIRMAN

Mr Justin Bruce
TREASURER

Mrs Andrea Alexander
SECRETARY

Professor Ursula Kees

Mr Michael Parker

Mr Allan Godfrey

Founder

Mr Peter Harper

Life Members

Mr Philip Bruce | Mr Geoffrey Cattach, AM | Mr Peter Falconer, OAM
Mr Peter Harper | Professor Ursula Kees | Mr Kim Williamson

Administration Staff

Mrs Andrea Alexander
CHIEF EXECUTIVE OFFICER

Mrs Kylie Dalton
HEAD OF DEVELOPMENT

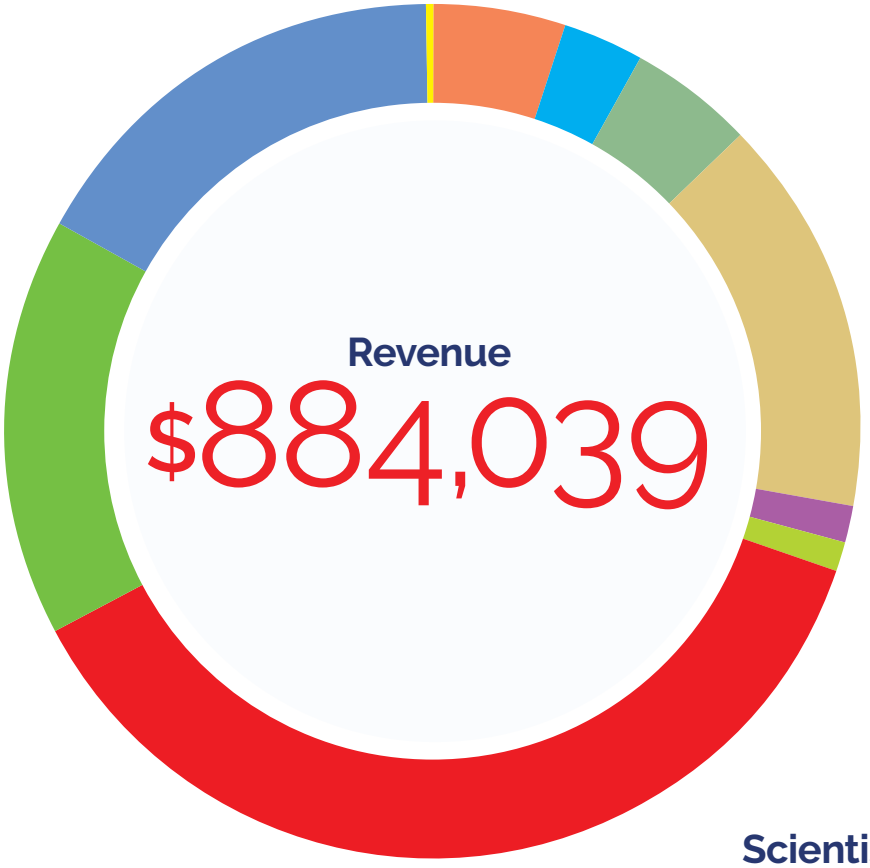
Mrs Wendy Kearns
EXECUTIVE OFFICER

Ms Sophie Galati
COMMUNICATIONS COORDINATOR

Ms Jody Williams
MARKETING MANAGER

Ms Lavanya Nadarajah
DONOR/FUNDRAISING SPECIALIST
(Resigned September 2021)

Stats & Achievements



Subscriptions	$1,711
Interest Received	$43,156
ATO Cash Boost Payments	$27,070
Jobkeeper Payments	$42,000
Gifts in Will	$133,266
Commercial Support	$11,998
Schools & Associations	$9,255
Raffles & Direct Mail Campaigns	$327,088
Community Activities	$139,236
Donations & Promotions	$149,259

Total research funded

More than

$1.06m

Scientists Supported

28

11 Rishi/Laurence's team
(2 PhD students, 1 Honours student)

7 Sébastien's team
(1 PhD student, 2 Honours students)

5 Joost's team
(2 PhD student)

5 Terry's team

Scientific Publications

10

Community Activities & Events

Almost

$140k Raised

Why Research Childhood Cancer?

Almost

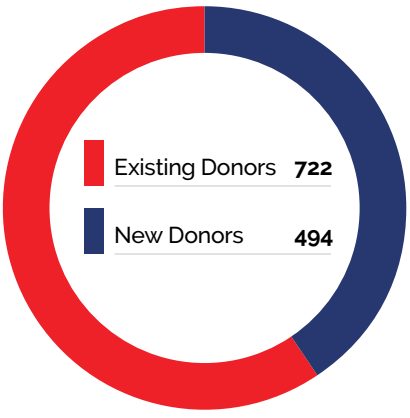
1k children and adolescents (0–19) diagnosed with childhood cancer every year in Australia

3 children a week lose their battle to cancer in Australia

Donations

Average $264

Previous $229



Funding of Grants

Triennial Block Grant (2019–2021)

(January–June 2021) **Total Expenditure:** $357,357

Researchers: Dr Rishi S Kotecha and Dr Laurence C Cheung

Title: *Identifying Novel Translatable Therapeutics for Infant Acute Lymphoblastic Leukaemia.*

Title: *Novel Therapeutics for Children with Leukaemia: Understanding and Targeting the Bone Marrow Microenvironment.*

CLCRF Ursula Kees Fellow (2017–2021)

(January–June 2021) **Total Expenditure:** $150,194

Researcher: Dr Sébastien Malinge

Title: *To develop new tools to identify cancer cells resistant to current therapy and test a new drug therapy to destroy them.*

Program Manager: Ms Emma Stone

(January–June 2021) **Total Expenditure:** $55,746

This amount was paid in the 2019/2020 financial period, but was reflective of research being funded by the CLCRF Telethon $1M partnership from July to December 2020. This was funding for the Triennial Block Grant and the CLCRF Ursula Kees Fellow grants.

Channel 7 Telethon Trust

Total Expenditure: $500,000

This amount was paid in the 2019/2020 financial period, but was reflective of research being funded by the CLCRF Telethon $1M partnership from July to December 2020.

*Telethon Grants Partnership — Oncogenic Signalling Laboratory

(July–December 2020) **Total Expenditure:** $148,269

Researcher: Professor Terry Johns

Title: *Development of a new and effective therapy against Diffuse Intrinsic Pontine Giloma*

*Sarcoma Program — Co-funded by CLCRF and The Abbie Basson Sarcoma Foundation

(July–December 2020) **Total Expenditure:** $10,371

Researcher: Dr Joost Lesterhuis

Title: *A new treatment to prevent sarcoma relapse after surgery*

*These research projects were supported by the additional funding from Telethon (enabled by CLCRF's $1M partnership in 2020) directly to the Telethon Kids Institute.

Total research funded

More than

$1.06m

Scientists Supported

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(2 PHD STUDENTS, 1 HONOURS STUDENT)

7 Sébastien's team
(1 PHD STUDENT, 2 HONOURS STUDENTS)

5 Joost's team
(2 PHD STUDENTS)

5 Terry's team

Community Activities & Events

The WA community and businesses continued to be generous during the year with over $139,236 raised from activities.

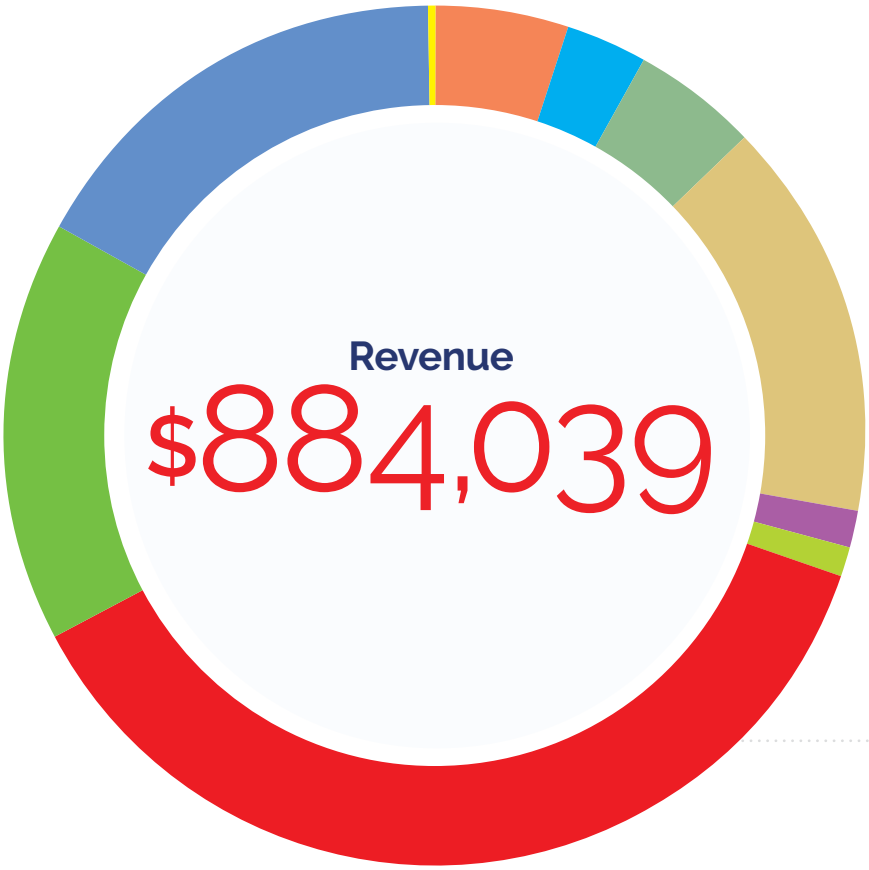
The WA community and businesses continued to be generous during the year with over $139,236 raised from activites such as the CLCRF Quiz Night/s, merchandise sales, 40K in 40Days Campaign, Entertainment Book sales, head shaves, fetes, annual kayak paddles, first birthday celebrations, annual Boar Swamp campdraft, school walkathon, Aust Day BBQ and support from Rotary and Lions clubs (just to name a few). Many of these have been reported on in our newsletters, EDM's and social media posts during the past 12 months.

One particular event that needs to be mentioned is the annual South West Bike Trek. The trek has been running for many years and we are indebted to Eric & Annette Maddock for organising the ride, the cyclists who undertook the 600km trek, the various service clubs and the many people who support this event every year. A total of $37,186 was raised.

Community Activities & Events

Another area of revenue was the raffles and direct mail campaigns. A net profit of $163,375 was made from three raffles and the annual Tax and Christmas appeals. Our thanks to Royal Life Saving Society of WA for their support with these activities.

The below image gives an indication as to where the majority of the Foundation's revenue during 2020/2021 was generated.



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Our Patron & Our Ambassador

We are delighted that Justin Langer, our inaugural Patron has agreed to continue his role as Patron of the Foundation for 2022.

Georgia Lowry is also continuing as an Ambassador for the Foundation. With Justin and Georgia's help they provide a public and community awareness of the Foundation.

GEORGIA LOWRY
CLCRF AMBASSADOR

The Foundation Team

The Foundation family grew in early 2021 with the appointment of Lavanya Nadarajah as our Donor Fundraising Specialist and Jody Williams as Marketing Manager.

The team have done a great job with working in such close quarters and have instigated a number of new campaigns to promote awareness of the Foundation and in due, course, increase financial support. Pictured below with Ms Celia Hammond MP.

Gifts in Wills/Endowment Fund

During the year the Foundation received $133,266 from Gifts in Wills and an Endowment Fund.

With the exception of the endowment fund donation, the Foundation was unaware of these gifts until the benefactors had passed.

+ **Manley Dawn**
+ **Bransden Jean**
+ **Lee Winifred**
+ **Longmore Violet**
+ **Margaret Stevenson Endowment Fund**

Total gifts

More than

$130k

Benefactors

+ **John & Janet Hughan:** $70,000
+ **Stan Perron Charitable Foundation:** $45,000
+ **Tate Family Foundation:** $25,000

Our continued thanks to these very generous supporters for their ongoing support of the Foundation over many years.

Corporate Benefactors

Support during the year continued to come from a number of corporate benefactors — **Toolmart** via the 2021 Tradies Expo, **Beyond Bank** with the Community Reward Payment and **Woolworths Group Ltd**.

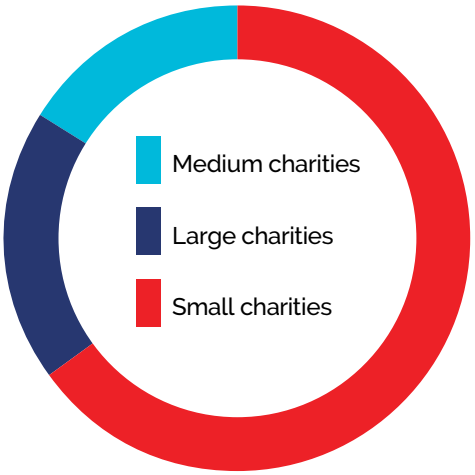
Conclusion

NATIONAL CHARITIES — 2019 Australian Charities Report:

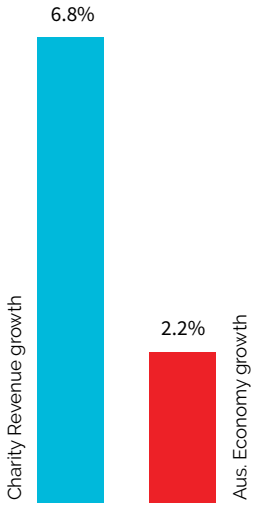
+ Australia's charities were predominantly based in major cities — state capitals and cities with populations of more than 100,000.
+ Charity revenue grew by 6.8% — significantly more than the 2.2% growth of the Australian economy in the same period.
+ Australia's charities, overall operated at a surplus, supported by substantial assets
+ Revenue was $166 billion in 2019 — an increase of $10.5 billion.
+ Donations rose to $11.8 billion in the 2019 reporting year — an increase of $1.3 billion from the previous year.
+ Assets increased by $30 billion to $354 billion.
+ Revenue from goods and services increased by $3.5 billion to $56.7b.
+ Government funding accounted for $78.1 billion, an increase of $4.4b.
+ Small charities (annual revenue less than $250,000) made up 65% of the sector, large charities (annual revenue of $1 million or more) made up 19% and medium charities (annual revenue of $250,000 to $999,000) made up 16%.
+ Charities employed 1.38 million people — approximately 11% of total employment in Australia.
+ Volunteer numbers decreased by approximately 200,000 to 3.6 million.
+ More than half of all charities (51%) operated without any paid staff.
+ Charities spent $85.9 billion on employee expenses, up 6% on the previous year's figure of $81.1 billion.
+ The most common activities for charities were religious activities and primary and secondary education.

Source: Australian Charities Report — 7th edition | Australian Charities and Not-for-profits Commission (acnc.gov.au)

Charity Sector Share

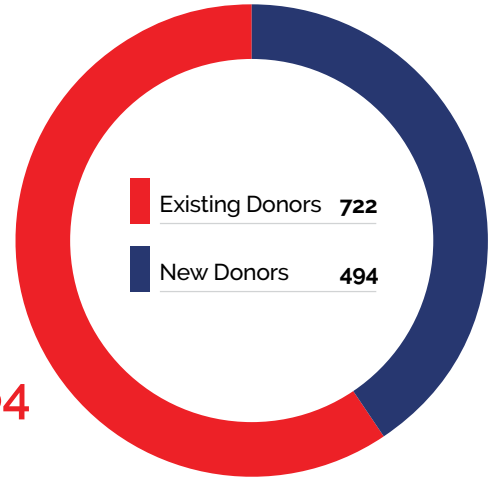


Revenue Comparison



Donations

During the 2020/2021 period, the Foundation received donations from 494 new donors and 722 existing donors. Whilst these figures are slightly down on last year, the average donation being of $264 is up from the previous year.



Average $264
Previous $229

Children's Leukaemia & Cancer Research 2020/2021

Telethon Kids Cancer Centre

OVERVIEW 2020/2021

The Telethon Kids Cancer Centre has had another amazing year! We are building a critical mass of childhood cancer researchers in Western Australia, with continued growth of our dedicated and talented team. Our growth is driven by our strong reputation for both research excellence and being a rewarding place to work and study. Our individual teams have demonstrated success in securing competitive funding for their research projects and have published new research results in high-quality scientific journals. These achievements are highlighted in the individual research reports to follow.

As a Centre, we were also successful in securing Centre-wide funding from the Telethon Trust for an exciting new collaborative research initiative. This was only possible thanks to decades of support from CLCRF, which has enabled us to build a platform of consistent, high-quality research outputs. The result has been the establishment a world-first pipeline of child-specific laboratory cancer models. These will revolutionise the development of new cancer therapies that are precisely targeted towards children. Our research focus is to use these game-changing models to develop more effective and safer childhood cancer therapies. These will be in the form of cancer immunotherapies - using the bodies' own immune system to fight the cancer and personalised medicines – using detailed genetic analysis to precisely target drugs to individual children.

We strongly believe that collaboration is the key to achieving research breakthroughs and as such we are incredibly excited by our growing collaborations, both within the Centre and externally. During the year, we have recruited a Core Research group to work across all of our teams, including an early career researcher, research assistants, casual laboratory technicians, and computational biologists. This has boosted our existing collaborative research program across the Centre and given each team an additional level of support.

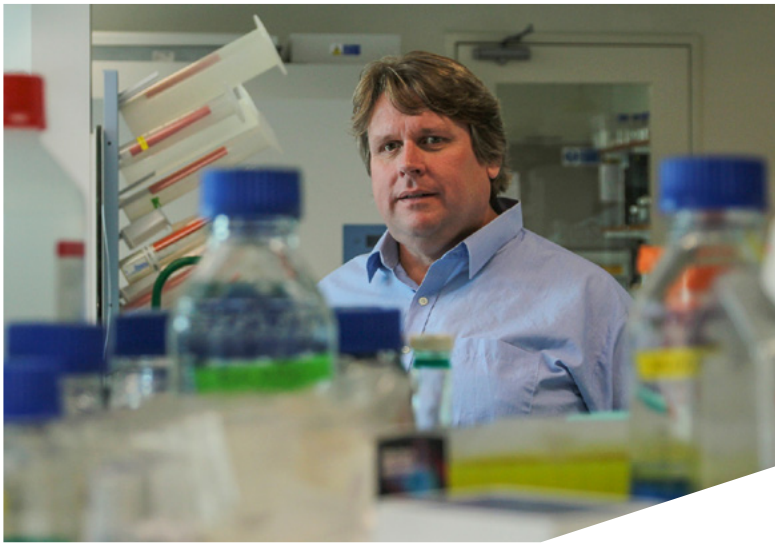
Throughout the year, we have also continued to build our vital collaboration and integration with the Perth Children's Hospital oncology unit. Our goal is to build Australia's first Comprehensive Kids Cancer Centre, to enable the seamless integration of research and clinical practice. This will truly give the best possible chance to children battling cancer in Western Australia.

The Centre continues to be supported by our CLCRF-funded Program Manager and we have recently recruited a Project Support Coordinator to help with additional administrative tasks. Together they ensure the daily operations of the Cancer Centre run smoothy, freeing up our team members to focus on their vital research. Our Program Manager also contributes towards strategy and its implementation, with a strong focus on finances and ongoing funding.

As a Centre, we are passionate about developing our up-and-coming future scientific leaders. We have now established working groups for both our students and early career postdoctoral researchers. The groups meet monthly in the form of workshops, pitch sessions, and social events. Our more senior team members also provide ongoing mentoring to drive career growth.

At the Telethon Kids Cancer, we are all up for the fight against childhood cancer! This would not be possible without the continued financial support from CLCRF and you, their supporters. You are joining us in our vision to defeat childhood cancer and to reduce the devastating long-term side effects of current treatments. Together, we are committed to making a difference to the lives of children currently fighting cancer and those yet to face a cancer diagnosis.

Professor Terrance Johns
DIRECTOR, TELETHON KIDS CANCER CENTRE



Funding: Triennial Block Grant (2019–2021)
Researchers: Dr Rishi S Kotecha and Dr Laurence C Cheung

2021 has been a year of positive change. The first of these has been to expand the capacity for leukaemia research within the Telethon Kids Cancer Centre through development of two research groups, namely Leukaemia Translational Research and Translational Genomics in Leukaemia. This has led to an increased breadth of research to be conducted in Western Australia for paediatric leukaemia, by allowing the research direction for each group to align with the individual strengths of the group heads, while at the same time using each of the group heads distinct strengths to maintain and promote collaboration between the groups.

As a result, 2021 has seen Dr Laurence Cheung successfully progress to Co-Head the Leukaemia Translational Research team alongside Dr Rishi Kotecha. The team has increased its capacity with recruitment of two post-doctoral officers, Dr Vincent Kuek and Dr Sung-Kai Chiu. Joyce Oommen, Sajla Singh, Emanuela Ferrari and Grace-Alyssa Chua continue as ever faithful research assistants and supervision and mentoring of the next generation of researchers continues through the groups' PhD candidates, Anastasia Hughes, Taylor Ferguson, and Nick Peters.

Sadly, in 2021 we had to farewell some of our most treasured team members, Jette Ford and Stewart Cattach. Jette retired after a 37-year career which changed the face of cancer research around the world through generation of over 100 unique patient-derived cell lines. Stewart's outstanding work as a laboratory technician, in addition to his endearing persona, has been sorely missed by the whole team. Despite these losses, and in the face of the COVID-19 pandemic, 2021 remained a successful year for the Leukaemia Translational Research team, as detailed below.

Module 1: Identifying Novel Translatable Therapeutics for Infant Acute Lymphoblastic Leukaemia

Acute lymphoblastic leukaemia is the most frequently occurring type of childhood leukaemia. International research over the past seventy years has led to massively improved cure rates. Around 90% of children and adolescents with acute lymphoblastic leukaemia can expect to be cured of their disease. In sharp contrast, newborns and babies who are less than 12 months of age at diagnosis face a dismal outlook. Translocations of the KMT2A (MLL) gene are present in up to 80% of ALL cells from infants, with 5-year event-free survival of less than 40%.

In an attempt to find better treatment for these infants, international study groups have conducted many therapeutic studies with more intensive therapy. Unfortunately, this led to a large number of toxic deaths and did not improve overall survival. Novel therapies are urgently required to improve outcomes.

Through our work, we have developed a preclinical testing pipeline to provide a comprehensive assessment of novel drug candidates that can be readily translated to the clinic. In prior years we have investigated romidepsin and gemcitabine, with the positive published findings from our experimental work indicating that these novel drug candidates would be suitable for integration into clinical trials for infants with KMT2A-rearranged acute lymphoblastic leukaemia.

In 2021, our primary research focus centred on whether a drug called carfilzomib could be effective for infants with KMT2A-rearranged acute lymphoblastic leukaemia. This drug was selected for investigation after it scored highly in an initial high throughput drug screen on our unique panel of cell lines derived from infants with KMT2A-rearranged leukaemia.

The results from our study identified that while carfilzomib was very effective in our cell line models, this benefit did not extend to our in vivo models. Despite the negative result, the significance of this study cannot be understated as it was able to show that in vitro efficacy does not necessarily translate into benefit in vivo. It highlighted the importance of in vivo validation prior to suggesting an agent for clinical use and most importantly, this study will allow prioritisation of more promising drug candidates and spare the unnecessary investigation of carfilzomib in a clinical trial for infants with KMT2A-rearranged acute lymphoblastic leukaemia.

The work within this research module has received long standing support by the Children's Leukaemia and Cancer Research Foundation and has generated a number of research publications and allowed us to leverage additional funding to support the work. These details are provided below.

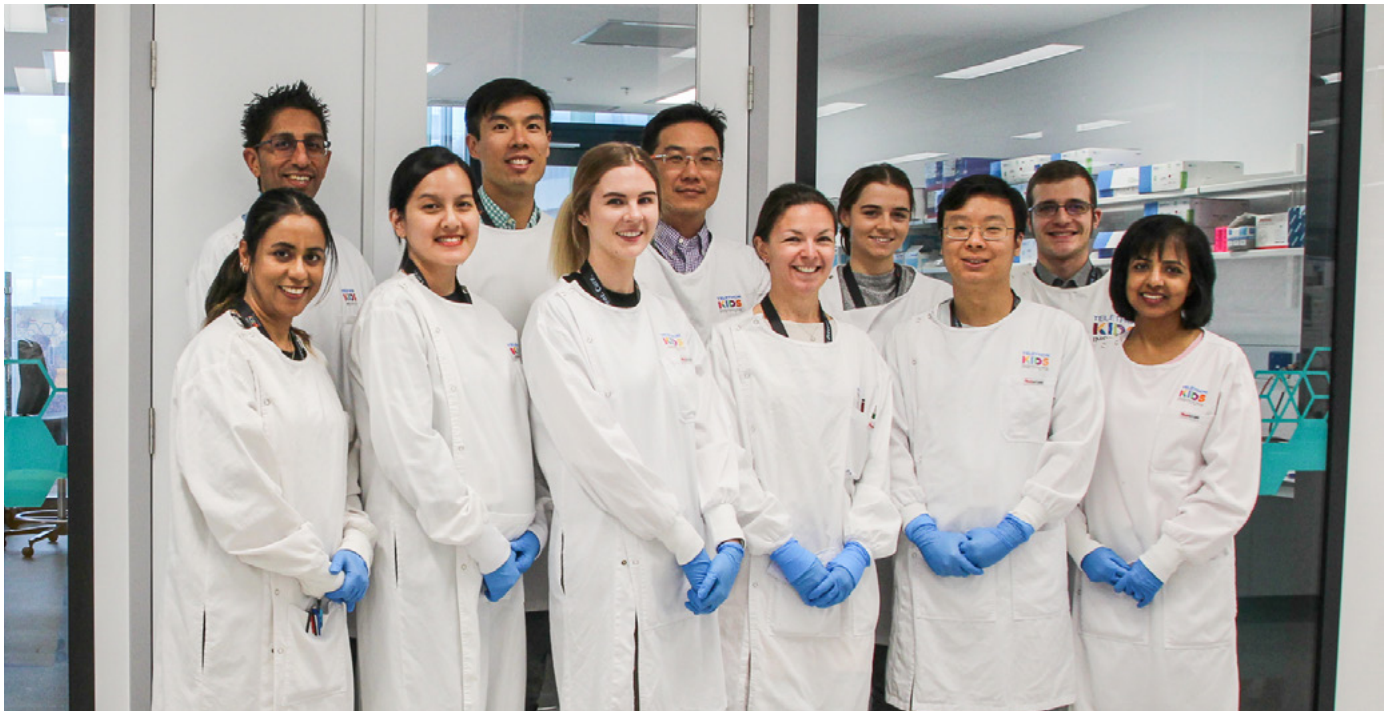
Additional Funding Leveraged

- Perpetual IMPACT Philanthropy Grant (2021): Preclinical drug-testing pipeline to evaluate the efficacy of PARP inhibitors for infants with acute lymphoblastic leukaemia (Kotecha RS, $143,908)
- Cancer Council Western Australia Collaborative Cancer Grant Scheme (2021): Testing PARP inhibitors to treat high-risk infant acute lymphoblastic leukaemia (Chiu SK, Gunosewoyo H, Kotecha RS, Cheung LC, $64,983)
- National Health and Medical Research Council Early Career Fellowship (2018-2021): Combinatorial Therapeutics in High-Risk Infant Acute Lymphoblastic Leukaemia (Kotecha RS, $344,657)

Relevant Publications

- Breese EH, Kotecha RS, Guest EM. Acute lymphoblastic leukemia in infants: A distinctive, high risk subtype of childhood ALL. In Litzow MR, Raetz EA, ed. Acute Lymphoblastic Leukemia: Translational Science and Clinical Management for Children and Adults from the Bench to the Bedside. Springer 2021 [Accepted].
- Stutterheim J, de Lorenzo P, van der Sluis I, Alten J, Ancliffe P, Attarbaschi A, Averso L, Boer J, Biondi A, Brethon B, Campbell M, Cazzaniga G, Escherich G, Ferster A, Gardner R, Kotecha RS, Lausen B, Li CK, Locatelli F, Rubnitz J, Silverman L, Stary J, Szczepanski T, van der Velden VHJ, Vora A, Schrappe M, Valsecchi MG, Pieters R. Outcome and prognostic significance of minimal residual disease in infants with KMT2A-germline acute lymphoblastic leukemia treated on the Interfant-06 protocol. European Journal of Cancer 2021 [Accepted].
- Symeonidou V, Jakobczyk H, Bashanfer S, Malouf C, Fotopoulou F, Kotecha RS, Anderson RA, Finch AJ, Ottersbach K. Defining the fetal origin of MLL-AF4 infant leukemia highlights specific fatty acid requirements. Cell Reports 2021;37(4):109900.
- Cheung LC, De Kraa R, Oommen J, Chua GA, Singh S, Hughes AM, Ferrari E, Ford J, Stam RW, Kees UR, Malinge S, Kotecha RS. Preclinical evaluation of carfilzomib for infant KMT2A-rearranged acute lymphoblastic leukemia. Frontiers in Oncology 2021;11:631594.
- Stutterheim J, Van der Sluis IM, De Lorenzo P, Alten J, Ancliffe P, Attarbaschi A, Brethon B, Biondi A, Campbell M, Cazzaniga G, Escherich G, Ferster A, Kotecha RS, Lausen B, Li CK, Lo Nigro L, Locatelli F, Marschalek R, Meyer C, Schrappe M, Stary J, Vora A, Zuna J, Van der Velden VHJ, Szczepanski T, Valsecchi MG, Pieters R. Clinical implications of minimal residual disease detection in infants with KMT2A-rearranged acute lymphoblastic leukemia treated on the Interfant-06 protocol. Journal of Clinical Oncology 2021;39(6):652-662.
- Wander P, Cheung LC, Pinhancos SS, Jones L, Kerstjens M, Arentsen-Peters STCJM, Singh S, Chua GA, Castro PG, Schneider P, Dolman MEM, Koopmans B, Molenaar JJ, Pieters R, Zwaan CM, Kotecha RS,* Stam RW.* Preclinical efficacy of gemcitabine in MLL-rearranged infant acute lymphoblastic leukemia. Leukemia 2020;34(11):2898-2902.
- Cheung LC, Cruikshank MN, Hughes AM, Singh S, Chua GA, Ford J, Ferrari E, Oommen J, Malinge S, Lock RB, Kees UR, Kotecha RS. Romidepsin enhances the efficacy of cytarabine in vivo, revealing histone deacetylase inhibition as a promising therapeutic strategy for KMT2A-rearranged infant acute lymphoblastic leukemia. Haematologica 2019;104(7):e300-e303
- Pieters R, De Lorenzo P, Ancliffe P, Aversa LA, Brethon B, Biondi A, Campbell M, Escherich G, Ferster A, Gardner RA, Kotecha RS, Lausen B, Li CK, Locatelli F, Attarbaschi A, Peters C, Rubnitz JE, Silverman LB, Stary J, Szczepanski T, Vora A, Schrappe M, Valsecchi MG. Outcome of infants younger than 1 year with acute lymphoblastic leukemia treated with the Interfant-06 protocol: results from an international phase III randomized study. Journal of Clinical Oncology 2019;37(25):2246-2256.
- Cruickshank MN, Ford J, Cheung LC, Heng J, Singh S, Wells J, Failes TW, Arndt GM, Smithers N, Prinjha RK, Anderson D, Carter KW, Gout AM, Lassmann T, O'Reilly J, Cole CH, Kotecha RS, Kees UR. Systematic chemical and molecular profiling of MLL-rearranged infant acute lymphoblastic leukemia reveals efficacy of romidepsin. Leukemia 2017;31(1):40-50.
- Kotecha RS, Gottardo NG, Kees UR, Cole CH. The evolution of clinical trials for infant acute lymphoblastic leukemia. Blood Cancer Journal 2014;4:e200.
- Kotecha RS, Ford J, Beesley AH, Anderson D, Cole CH, Kees UR. Molecular characterization of identical, novel MLL-EPS15 translocation and individual genomic copy number alterations in monozygotic infant twins with acute lymphoblastic leukemia. Haematologica 2012;97(9):1447-1450.
- Kotecha RS, Murch A, Kees U, Cole CH. Pre-natal, clonal origin of t(1;11)(p32;q23) acute lymphoblastic leukemia in monozygotic twins. Leukemia Research 2012;36(1):46-50.

Module 2: Novel Therapeutics for Children with Leukaemia: Understanding and Targeting the Bone Marrow Microenvironment



Skeletal abnormalities are common in children with leukaemia, with over 35% of patients suffering from musculoskeletal pain at diagnosis. Development of leukaemia causes bone destruction with bone scan assessments showing that the bone volume and the thickness of the bone are lower than normal prior to initiating chemotherapy.

Furthermore, bone marrow biopsies performed to diagnose children with leukaemia revealed that there are fewer fat cells and bone-forming cells than normal, yet little is known about the contribution of bone marrow cells during disease development, at progression and at relapse.

Within this module, we conducted a study of the bone cells and bone marrow cells during leukaemia development. In 2018, we successfully developed a novel preclinical model that allows comprehensive investigation of the bone cells and surrounding normal cells in the bone marrow during leukaemia development. Importantly, this model faithfully replicates human disease and the clinical symptoms of increased bone fragility and reduced bone mineral density in children with a diagnosis of ALL.

We first investigated development of the disease in our model system and monitored each population of the neighbouring normal cells. We could clearly show that during the initial phases the leukaemia cells did not expand, however the neighbouring environment was remodelled to facilitate the subsequent support of the cancerous growth. Notably, the normal production of blood cells and immune cells in the bone marrow were affected during leukaemia development.

In 2020, we compared the gene expression profiles of cells from the leukaemic bone marrow to the normal cells using the latest single cell sequencing technologies. The findings from this study extended our understanding of the complexity of changes and cell-cell interactions among the normal cells of the bone marrow environment during leukaemia progression. Our ultimate goal is to identify the 'bad' bone marrow cells so that we can develop treatments to disrupt the interactions between the leukaemia cells and 'bad' neighbouring cells in the bone marrow.

We further discovered that bone-eating cells are highly active, resulting in bone loss during leukaemia development. We therefore hypothesised that restoration of the healthy bone marrow environment has the potential to reduce leukaemia progression and improve treatment outcomes.

In 2019, we tested an inhibitor of bone-eating cells, zoledronic acid, which has the capacity to reduce bone loss in patients with other conditions. We found that

treatment with zoledronic acid reduced leukaemia progression and extended survival in our model. In 2020, we showed that zoledronic acid improved treatment outcome when combined with currently used chemotherapeutic drugs. Unlike chemotherapeutic drugs, zoledronic acid is safe and well tolerated by children, and is already in clinical use in children for a wide variety of other indications.

Our findings suggest that restoration of the normal environment in the bone marrow to control cancer progression is a promising therapeutic avenue. Currently, we are investigating the role of marrow stem cells, fat cells and bone-forming cells during leukemia development with the aim to identify additional new therapeutic targets for children with leukaemia.

The work within this research module has received long standing support by the Children's Leukaemia and Cancer Research Foundation and has generated a number of research publications and allowed us to leverage additional funding to support the work. These details are provided below.

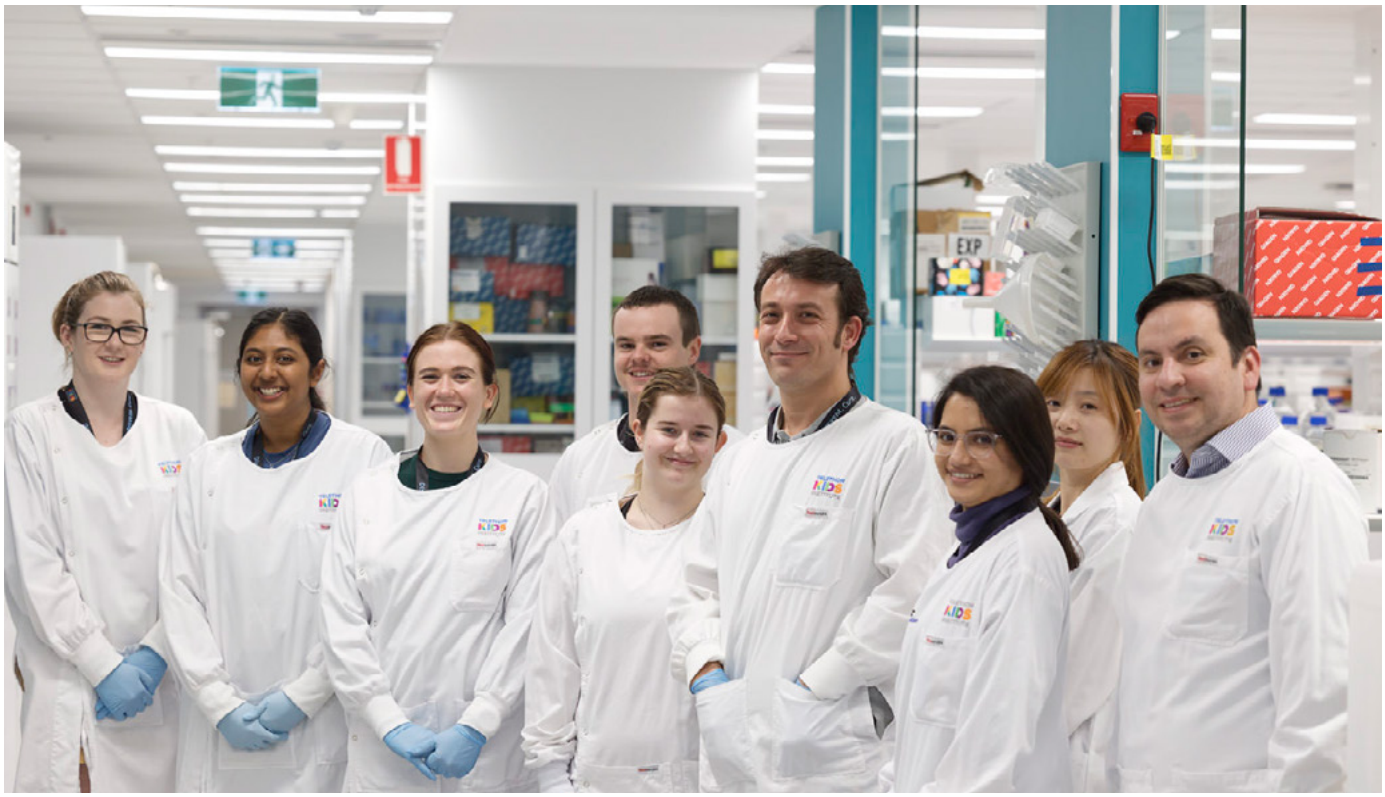
Additional Funding Leveraged

- Cancer Australia Priority-driven Collaborative Cancer Research Scheme (PdCCRS) (2021-2022): New therapeutic strategies for children with high-risk leukaemia by dissecting and targeting the bone marrow microenvironment (Cheung LC, $199,530)
- Tour de Cure Young Researcher Research Grant (2019-2020): New therapeutic opportunities by targeting the bone marrow microenvironment of high-risk childhood leukaemias (Cheung LC, $98,020)
- Perth Children's Hospital Foundation Project Grant (2018-2020): Exploiting the use of zoledronic acid to improve the outcome in childhood leukaemia (Cheung LC, Kotecha RS, Tickner J, $78,554)

Relevant Publications

- Kuek V, Hughes AM, Kotecha RS, Cheung LC. Therapeutic targeting of the leukemia microenvironment. International Journal of Molecular Sciences 2021;22(13):6888.
- Anderson D, Skut P, Hughes AM, Ferrari E, Tickner J, Xu J, Mullin BH, Tang D, Malinge S, Kees UR, Kotecha RS,* Lassmann T,* Cheung LC.* The bone marrow microenvironment of pre-B acute lymphoblastic leukemia at single-cell resolution. Scientific Reports 2020;10(1):19173.
- Kotecha RS, Cheung LC. Targeting the bone marrow microenvironment: a novel therapeutic strategy for pre-B acute lymphoblastic leukemia. Oncotarget 2019;10(19):1756-1757.
- Cheung LC, Tickner J, Hughes AM, Skut P, Howlett M, Foley B, Oommen, J, Wells JE, He B, Singh S, Chua GA, Ford J, Mullighan CG, Kotecha RS,* Kees UR.* Dissecting the pre-B leukemia bone marrow microenvironment reveals new therapeutic opportunities. Leukemia 2018;32(11):2326-2338.
- Wells JE, Howlett M, Halse HM, Heng J, Ford J, Cheung LC, Samuels AL, Crook M, Charles AK, Cole CH, Kees UR. High expression of connective tissue growth factor accelerates dissemination of leukaemia. Oncogene 2016;35(35):4591-4600.
- Wells JE, Howlett M, Cheung LC, Kees UR, 2015. The role of CCN family genes in haematological malignancies. Journal of Cell Communication and Signaling 2015;9(3):267-278.
- Cheung LC, Strickland DH, Howlett M, Ford F, Charles AK, Lyons KM, Brigstock DR, Goldschmeding R, Cole CH, Alexander WS, Kees UR. Connective tissue growth factor is expressed in bone marrow stromal cells and promotes interleukin-7-dependent B lymphopoiesis. Haematologica 2014;99(7):1149-1156.

Funding: CLCRF – Ursula Kees Fellow (2017–2021)
Researcher: Dr Sébastien Malinge
Title: To develop new tools to identify cancer cells resistant to current therapy and test a new drug therapy to destroy them



Acute Leukaemia is the most common type of cancer seen in children, accounting for 30% of all paediatric cancers worldwide. In Australia, it is estimated that more than 240 children aged 0-14 years will be diagnosed with leukaemia each year. Overall, the survival of children with leukaemia has significantly improved over the past few decades with more adapted treatments, with current 5-year overall survival approaching 90% for acute lymphoblastic leukaemia (ALL).

Despite this success, leukaemia remains the second cause of death by cancer in children. Many kids continue to have a poor prognosis, suffering from relapse and treatment related toxicity, which can lead to increased mortality and necessitate longer hospital admissions and ongoing care.

Current therapeutic approaches have now reached their maximum potential, highlighting the need for new, efficacious, more targeted, and less toxic treatments.

Through a better understanding of leukemia development, response to treatment, mechanisms of resistance to therapy and relapse initiation, our overarching goal is to discover new cellular and molecular targets and develop novel personalised treatments with increased efficacy and less toxicity, to improve long term outcomes and quality of care for children with leukaemia.

Our research is mostly focused on children with Down sSndrome (DS) because these kids are at a higher risk of developing leukaemia, have a higher rate of treatment toxicity, and have a higher risk of relapse compared to other children. Using DS-leukemia as a disease model, we aim to uncover key mechanisms to better prevent, treat, and cure leukaemia in all children, not only those with Down Syndrome.

Over this year, we have achieved several key milestones:

Created new tools to drill down into leukaemia development

Through our ongoing collaborations with clinicians and several Australian biobanks, we have collected several leukaemia samples to characterise the mutations that are causing cancer. We are reproducing leukemia in test tubes to unveil the critical moment and critical cell type where leukemia originates. Building these new tools now offers us a platform to identify specific molecular weaknesses to develop new therapies that may be implemented to prevent leukaemia development and improve current treatments. This will facilitate a rapid translation of our research into clinical trials in Western Australia and across the world.

Tested the efficacy of a new drug targeting DYRK1A

Gain of chromosome 21 is one of the most common genetic alterations seen in childhood leukaemia, but little is known about its role in leukaemia development. Using our Down Syndrome models (that have three copies of chromosome 21), we identified DYRK1A as a key player in DS leukaemia development. In a collaborative effort, we tested the efficacy of a new drug that targets DYRK1A in test tubes and preclinical models. In brief, this study showed that DYRK1A inhibition improves the outcomes of our DS-ALL preclinical models by decreasing leukaemia burden and prolonging survival. As a follow up, we are now assessing the efficacy of using this DYRK1A inhibitor in combination with conventional treatments.

Developed a pipeline to understand resistance to treatment

Relapse is a main reason for treatment failure, and children with relapsed leukemia suffer from treatment toxicity due to treatment intensification. In most cases, relapse originates from cancer cells that resist conventional therapy. These resistant cells are usually adaptive and are very rare, thus preventing us from developing targeted therapies. To bypass this limitation, we recently applied an integrative pipeline (multi-omic approach) to identify the key features of every individual leukemic cell that is resistant to treatment. In the near future, this will enable us to uncover novel actionable targets in the very few cells that resist treatment.

We strongly believe that this pipeline will be broadly applicable and will facilitate the development of new personalised therapies for childhood leukaemia such as immunotherapy.

Additional Funding Leveraged

- Jerome Lejeune Foundation (2021-2022): Symposium organisation (Malinge S, $46,185)
- Stan Perron Foundation (2020-2024): Paediatric Cancer Immunotherapy Program (co-CI Malinge S, $1,576,882)
- Australian Lions Childhood Cancer Research Foundation (2020-2023): Paediatric Cancer Immunotherapy for Australia (co-CI Malinge S, $1,050,000)
- Telethon Trust (2021): Creating Australia's Premier Children's Cancer Immunotherapy Research Program (co-CI Malinge S, $900,000)
- Jerome Lejeune Foundation (2021-2022): Exploratory grant (co-CI Malinge S, $61,595)
- Cancer Council Western Australia Project Grant (2021-2022) Towards preventing relapse in childhood leukaemia, (Malinge S, $99,023)
- Telethon Kids Cancer Centre (2020-2021): Internal grant (Malinge S, $22,500)
- Cancer Council Western Australia Research Fellowship (2020-2023): Towards targeting treatment-resistant cancer cells to prevent relapse in childhood leukaemia (Malinge S, $480,000)
- Jérome Lejeune Foundation Advanced Grant (2019-2021): Targeting DYRK1A: A Key Player in Down Syndrome Leukaemogenesis (Malinge S, $133,442)

Relevant Publications

- Dierssen M, Herault Y, Helguera P, Martínez de Lagran M, Vazquez A, Christian B, Carmona-Iragui M, Wiseman F, Mobley W, Fisher EMC, Brault V, Esbensen A, Jacola LM, Potier MC, Hamlett ED, Abbeduto L, Del Hoyo Soriano L, Busciglio J, Iulita MF, Crispino J, Malinge S, Barone E, Perluigi M, Costanzo F, Delabar JM, Bartesaghi R, Dekker AD, De Deyn P, Fortea Ormaechea J, Shaw PA, Haydar TF, Sherman SL, Strydom A, Bhattacharyya A. Building the Future Therapies for Down Syndrome: The Third International Conference of the T21 Research Society. Mol Syndromol. 2021 Jul;12(4):202-218.
- Cheung LC, de Kraa R, Oommen J, Chua GA, Singh S, Hughes AM, Ferrari E, Ford J, Chiu SK, Stam RW, Kees UR, Malinge S, Kotecha RS. Preclinical Evaluation of Carfilzomib for Infant KMT2A-Rearranged Acute Lymphoblastic Leukemia. Frontier in Oncology. 2021 Apr 15;11:631594.
- Bhansali RS, Rammohan M, Lee P, Laurent AP, Wen Q, Suraneni P, Tsai YC, Jenni S, Bornhauser B, Siret A, Fruit C, Pacheco-Benichou A, Harris E, Besson T, Thompson BJ, Goo YA, Hijiya N, Vilenchik M, Izraeli S, Bourquin JP, Malinge S, and Crispino JD. DYRK1A regulates B-ALL through phosphorylation of FOXO1 and STAT3. Journal of Clinical Investigation. 2021 Jan 4;131(1):e135937.
- Anderson D, Skut P, Hughes AM, Ferrari E, Tickner J, Xu J, Mullin BH, Tang D, Malinge S, Kees UR, Kotecha RS, Lassmann T, Cheung LC. The bone marrow microenvironment of pre-B acute lymphoblastic leukemia at single-cell resolution. Sci Rep. 2020 Nov 5;10(1):19173
- Laurent AP, Kotecha R and Malinge S. Gains of chromosome 21 in hematological malignancies: lessons from studying leukemia in children with down syndrome. Leukemia. 2020 May 20.
- Laurent AP, Siret A, Ignacimouttou C, Diop MB, Jenni S, Tsai YC, Ross-Weil D, Aid Z, Prade N, Plassard D, Pierron G, Daudigeos-Dubus E, Lecluse Y, Droin N, Bornhauser B, Cheung L, Crispino JD, Gaudry M, Bernard OA, Macintyre E, Barin Bonnigal C, Kotecha R, Goeorger B, Ballerini P, Bourquin JP, Delabesse E, Mercher T and Malinge S. Constitutive activation of RAS/MAPK pathway cooperates with trisomy 21 and is therapeutically exploitable in Down syndrome B-cell Leukemia. Clinical Cancer Research. 2020 Jul 1;26(13):3307-3318.
- Malinge S. SNAIL trail in myeloid malignancies. Blood. 2020 Aug 20;136(8):920-921.
- Cheung LC, Cruickshank MN, Hughes AM, Singh S, Chua GA, Ford J, Ferrari E, Oommen J, Malinge S, Lock RB, Kees UR, Kotecha RS. Romidepsin enhances the efficacy of cytarabine in vivo, revealing histone deacetylase inhibition as a promising therapeutic strategy for KMT2A-rearranged infant acute lymphoblastic leukemia. Haematologica. 2019 Jul;104(7):e300-e303.
- Lopez CK, Noguera E, Stavropoulou V, Robert E, Aid Z, Ballerini P, Bilhou-Nabera C, Lapillonne H, Boudia F, Thirant C, Fagnan A, Arcangeli ML, Kinston SJ, Diop M, Job B, Lecluse Y, Brunet E, Babin L, Villeval JL, Delabesse E, Peters AHFM, Vainchenker W, Gaudry M, Masetti R, Locatelli F, Malinge S, Nerlov C, Droin N, Lobry C, Godin I, Bernard OA, Göttgens B, Petit A, Pflumio F, Schwaller J, Mercher T. Ontogenic Changes in Hematopoietic Hierarchy Determine Pediatric Specificity and Disease Phenotype in Fusion Oncogene-Driven Myeloid Leukemia. Cancer Discovery. 2019 Oct 29.
- Rivera-Munoz P, Laurent A, Siret S, Lopez CK, Ignacimouttou C, Cornejo MC, Rameau P, Bernard OA, Dessen P, Gilliland GD, Mercher T and Malinge S. Partial trisomy 21 contributes to T cell malignancies induced by JAK3 activating mutations in murine models. Blood Advances 2018 Jul 10;2(13):1616-1627.

Funding: Program Manager
Manager: Ms Emma Stone
Title: Telethon Kids Cancer Centre Program Manager

Thanks to the generous support of CLCRF, I have had the privilege of being the Program Manager of the Telethon Kids Cancer Centre for over a year now. The team and I are grateful to CLCRF for recognising the importance of giving our hardworking researchers the additional support that they need.

Although my role can't be compared to the invaluable work our researchers are doing, every minute that I invest allows the researchers to get on with what they do best. That is, developing desperately needed new treatments to increase the chance of survival for children fighting cancer, whilst at the same time working to eliminate the horrendous life-long side effects caused by current therapies.

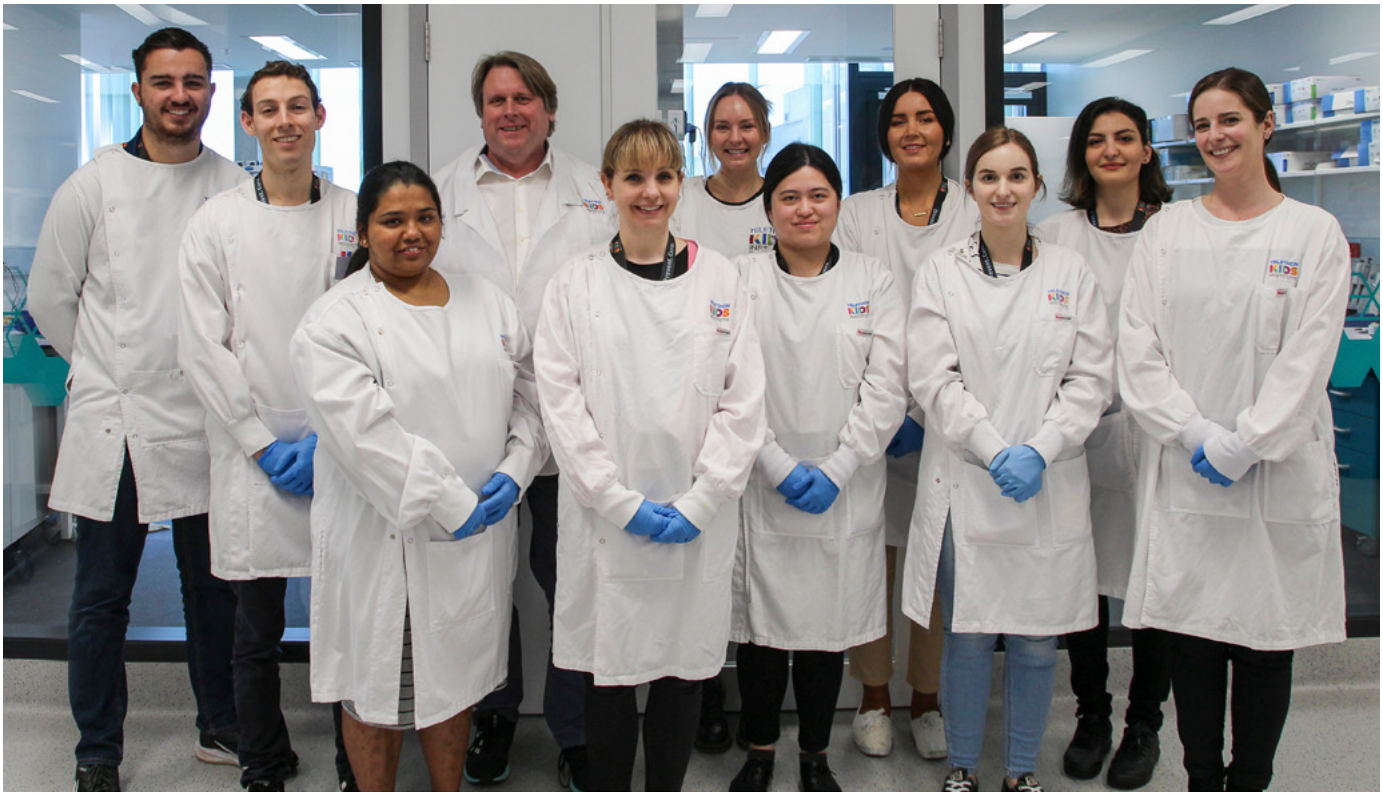
It has been an exciting year of growth for the Cancer Centre, not only in terms of the size of the team, but also in building exciting new pillars of research across the Centre – the development of world-first child-specific cancer laboratory models, together with the overarching themes of immunotherapy and personalised medicine. This growth has kept me incredibly busy, not only working with Prof Terrance Johns, Director of the Cancer Centre, to build and implement the strategy, but operationally in managing the day-to-day logistics. To assist with the increased administrative burden, we recently recruited Leisa Hudson as our Project Support Coordinator.

As the Centre's Program Manager, I see myself as the go-to-person for the team with the mission of "making things happen"! As a team, Leisa and I, drive and coordinate funding opportunities, provide financial management, provide administrative support, manage projects, support recruitment and retention of team members, assist with governance compliance, manage communications such as our website and social media, and offer vital stakeholder engagement, including with our Community Reference Group and supporters. This last point is a very important aspect of my role; working closely with CLCRF and other stakeholders to ensure that their needs and milestones are met. These tasks are all undertaken with significant support from the Institute's Professional Services teams.

I am delighted that CLCRFs ongoing financial support will allow me to continue as part of the remarkable Telethon Kids Cancer Centre team. I am committed to ensuring the continued smooth operations of the Centre over the coming year. Even more excitingly, I look forward to working towards exciting new initiatives, including our vision of becoming a Comprehensive Kids Cancer Centre, fully integrated with the Perth Children's Hospital oncology unit.

I give heartfelt thanks to CLCRF for entrusting me with this important position!

Funding: Telethon Grants Partnership – Oncogenic Signalling Laboratory
Researcher: Professor Terrance Johns
Title: Development of a New and Effective Therapy Against Diffuse Intrinsic Pontine Glioma



The main aim of this project is to identify novel therapies that will be effective in High Grade Glioma (HGG), a serious type of brain cancer in all age groups.

In children, our particular focus has been Diffuse intrinsic pontine glioma (DIPG), a 100% lethal form of HGG. Targeted therapy is a cancer-specific treatment that uses drugs that target specific molecules involved in the growth of cancers. Unfortunately, this approach has failed for DIPG to date, despite its success in other types of cancer.

Like normal brain cells, DIPG cells are "plastic" which means they can rapidly adapt to different conditions in their environment. When exposed to a targeted therapy, DIPG cells quickly adjust and become resistant to the drug. We hypothesised that this process of plasticity is driven by ion channels, which are pore-forming proteins that control the flow of small charged molecules (like sodium and potassium) in and out of the cell. These flows of ions can rapidly change the internal wiring of a cell. For this reason, ion channels have been associated with brain plasticity.

We hypothesised that using drugs that block the ion channels found in DIPG would prevent this plasticity, making targeted therapies more effective.

Our studies have made significant progress towards identifying ion channels found. DIPG, their function and how we might target them. Specifically, we have:

1) Used DIPG genetic databases to identify the ion channels found in patient samples. There are over 300 ion channels in humans and only a small number were found in DIPG.

2) Confirmed that the ion channels identified were actually present in patient samples and in our patient-derived DIPG cell lines.

3) Proved that these ion channels are functional in DIPG cells using a state-of-the-art technology called "patch clamping".

4) Used this information to identify ion channel drugs that might stop the growth of DIPG cells.

5) Found a combination of a targeted therapy and ion channel drug that shows significant promise as a treatment for DIPG.

Thus, we have made exciting progress in this entirely new field of research. Moving forward we plan to access this novel drug combination in animal models as the next step

of moving this towards the clinic. We have also commenced functional studies to try and understand how the ion channels help the DIPG cells to grow and survive. Finally, we are preparing a patent on our novel drug combination.

Additional Funding Leveraged

- Stan Perron Foundation (2020-2024): Paediatric Cancer Immunotherapy Program (Johns, TJ, $1,576,882)
- Australian Lions Childhood Cancer Research Foundation (2020-2023): Paediatric Cancer Immunotherapy for Australia (Johns, TJ, $1,050,000)
- Telethon Trust (2021): Creating Australia's Premier Children's Cancer Immunotherapy Research Program (Johns, TJ, $900,000)
- Western Australian Child Research Fund (2020-2022); Development of a new therapy against Diffuse Intrinsic Pontine Glioma (Johns, TJ, $249,945)
- Perth Children's Hospital Foundation (2019-2021); Development of a new therapy against Diffuse Intrinsic Pontine Glioma (Johns, TJ, $78,492)

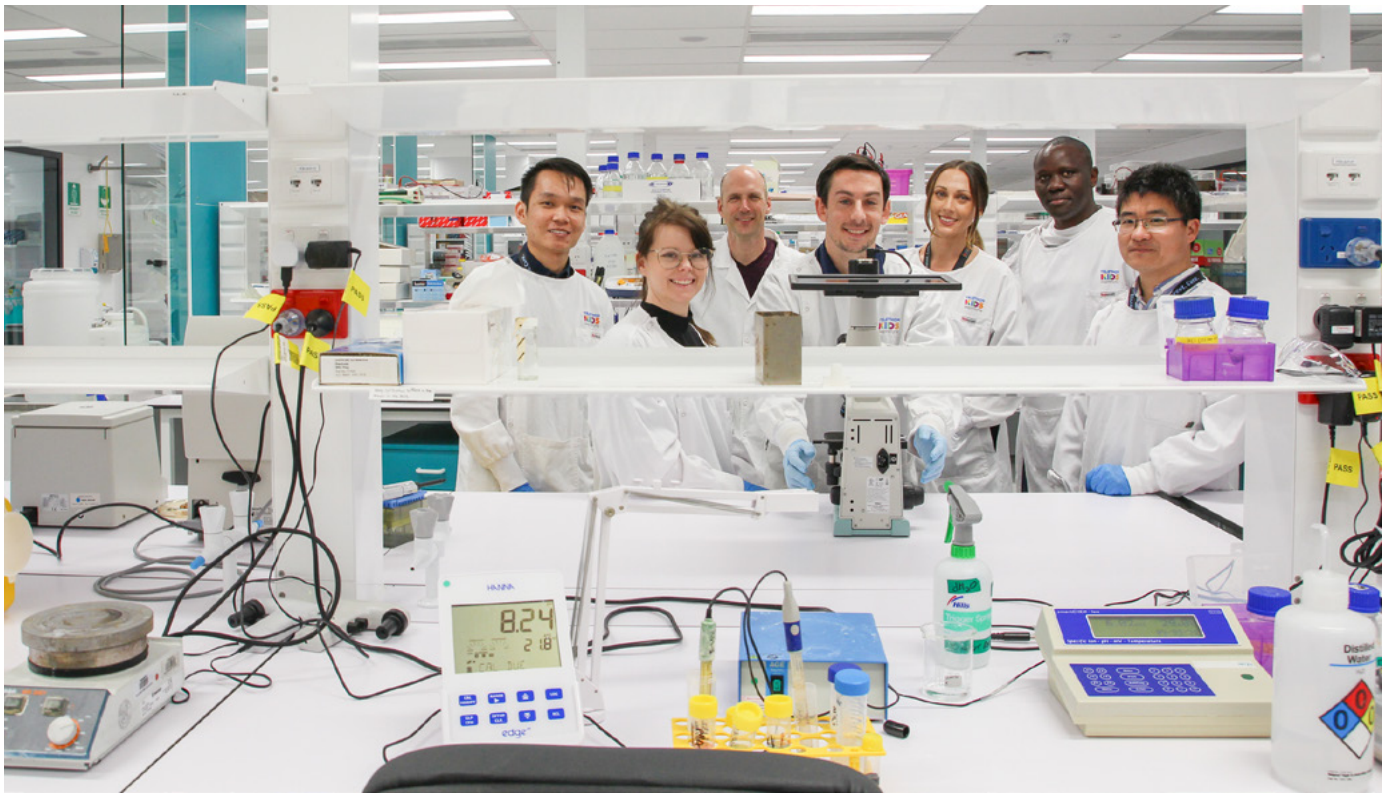
Relevant Publications

- Conference Presentation: International DIPG Symposium 2021, Invited Talk

Funding: Sarcoma Program – Co-funded by CLCRF and The Abbie Basson Sarcoma Foundation

Researcher: Dr Joost Lesterhuis

Title: A new treatment to prevent sarcoma relapse after surgery



Sarcoma is the third most frequent cancer in children and young people. Soft tissue sarcoma is a group of cancers derived from muscle, fat or connective tissues, characterised by local aggressive growth.

Current treatments of sarcoma can have severe side effects and large surgical procedures are often required in order to get complete resection of all cancer tissue. For sarcomas in limbs this not infrequently involves amputation. In addition, children will be treated with chemotherapy and/or radiotherapy to prevent relapse. Despite these aggressive treatments, the cancer recurs in approximately one third of the cases in high-risk soft tissue sarcoma in children. In adults, these percentages are even higher, for example around 50% in retroperitoneal sarcoma, with chemotherapy and radiotherapy providing little benefit, if any. Sarcoma is a particularly under-investigated cancer because it is relatively rare in adults (1% of cancers), thus receiving little interest from pharmaceutical companies. In children, however, sarcoma is the third most common cancer, representing about 15% of all cancers. More research is urgently needed as sarcoma prognosis and treatments have not changed in the last 20 years.

Our aim is to develop a biodegradable material that slowly releases immunotherapy drugs, which can be applied in the wound bed after surgical resection of soft tissue sarcoma. These drugs will attract and activate immune cells that can search and destroy remaining cancer cells, thus preventing the cancer from recurring. This is a unique approach that tackles a particular important problem in sarcoma; local recurrence after intensive surgery, despite aggressive treatments with sometimes severe long-term side effects. Our therapy provides hope for a treatment that is easy to use, that does not require additional treatments (the drug is released locally while the child goes through normal daily activities and after several weeks the biocompatible material is completely degraded) and does not come with severe side effects. The work in this project is the result of a unique collaboration between material scientists and cancer immunologists/oncologists.

Our aim was to have a prototype ready within 1-2 years that was optimised in preclinical models and that we could take forward into clinical trials to help pet dogs who naturally develop sarcoma. Because

we will then have evidence of safety and efficacy in two independent animal models (an FDA requirement), we hope we will be able to take the final leap into clinical trials in patients with sarcoma within several years' time. The results obtained in sarcoma may be translated to other cancers that often relapse after surgery, such as paediatric brain cancer and other solid tumours.

We have made excellent progress. We have made several iterations of a prototype gel, improving it along the way. We now have a gel that has the right consistency, the right degradation speed (it is completely taken up by the body in the right time frame), has the right release kinetics of the immunotherapy (it releases the drug over the desired period of time) and it is efficacious in preventing sarcoma from recurring, even when as much as 25% of the tumour is left behind after surgery. In addition, we have found that the wound healing response is not negatively affected by the gel, rather, it is actually enhanced.

We tested our gel in multiple preclinical sarcoma models, showing that it indeed was able to prevent cancer relapse when applied during surgery. We also tested its efficacy in combination with currently available immunotherapy antibodies, showing that the gel was able to turn sarcomas from a non-responsive into a responsive cancer. We also successfully incorporated a biomarker into the gel that allows us to measure the immune response induced by the gel, by simply taking a tube of blood from the mouse/dog/patient one or two weeks later. In the lab, we demonstrated that we can use this biomarker to optimise the dose when going to human clinical trials.

Building on the success of the gel approach, we are now testing several other immunotherapies to incorporate into the gel.

Lastly, we started a veterinary clinical trial in dogs with soft tissue sarcoma in collaboration with veterinary oncologist Dr Ken Wyatt from Perth Veterinary Oncology. We obtained ethics approval and expect to treat the first dog soon.

In addition to existing team members, A/Prof Joost Lesterhuis, post-doc Dr Rachael Zemek, post-doc Dr Ben Wylie and PhD students Francois Rwandamuriye and Breana Vitali, the Sarcoma Translational Research team at the Telethon Kids Cancer Centre was further expanded this year with the addition of post-doc (vet and chemist) Dr Tao Wang and research assistant Dat Nguyen (who will transition to a PhD in January 2023).

Additional Funding Leveraged

- NHMRC Investigator Grant (2021-2025): Tipping the balance - improving response rates to cancer immunotherapy (Lesterhuis WJ, $1,562,250)
- Cancer Australia/The Kids' Cancer Project (2020-2022): Intraoperative immunotherapy to prevent relapse in soft tissue sarcoma (Lesterhuis WJ, $395,050)
- Simon Lee Foundation (2020-2022): Grant for paediatric research (Lesterhuis WJ, $450,000)
- Australian Lions Childhood Cancer Research Foundation (2020-2023): Paediatric Cancer Immunotherapy Program (co-CI Lesterhuis WJ, $1.05m)
- Abbie Basson Sarcoma Research (2019-2022): Scholarship (Rwandamuriye B, Lesterhuis WJ, $30,000)
- Abbie Basson Sarcoma Research (2020-2022): Scholarship (Weston B, Lesterhuis WJ, $30,000)
- Cancer Council WA Collaborative Cancer Grant Scheme (2021-2022): Exploiting the healing process to stop cancer coming back after surgery (Zemek R, $64,600)
- Forrest Research Foundation (2021-2022): Prospect Fellowship (Zemek R, $142,500)

Relevant Publications

- Zemek RM*, Chin WL*, Fear V, Casey TH, Forbes C, Tilsed C, Boon L, Bosco A, Forrest AR, Millward MJ, Nowak AK, Lake RA, Lassmann T*, LESTERHUIS WJ * (Shared authors). Temporally restricted activation of IFNβ signaling determines response to immune checkpoint therapy. Nature Communications 2021, sent out for peer review.
- Tilsed CM, Principe, N, Kidman J, Chin WL, Zemek RM, Chee J, Islam R, Fear VS, Forbes C, Aston WJ, Jansen M, Chopra A, Lassmann T, Nowak AK, Fisher SA, Lake RA, LESTERHUIS WJ. CD4+ T cells drive an inflammatory, TNFα/IFN rich tumor microenvironment responsive to chemotherapy. Cell Reports 2021, sent out for peer review.
- Systematic investigation of chemotherapy and immune checkpoint blockade combinations in preclinical cancer models. Principe N, Aston WJ, Hope D, Tilsed CM, Fisher SA, Boon L, Dick IM, Chin WL, McDonnel AM, Nowak AK, Lake RA, Chee J*, LESTERHUIS WJ* (Shared authors). Journal for ImmunoTherapy of Cancer 2021, sent out for peer review
- Tilsed CM, Casey T, De Jong E, Bosco A, Zemek R, Salmons J, Wan G, MIllward MJ, Nowak AK, Lake RA, LESTERHUIS WJ. Retinoic acid induces an IFN-driven inflammatory tumour microenvironment, sensitizing to immune checkpoint therapy. Journal for ImmunoTherapy of Cancer 2021, sent out for peer review
- Zemek RM*, Fear F, Forbes C, De Jong E, Boon L, Casey T, Lassman T, Bosco A, Millward MJ, Nowak AK, Lake R, Lesterhuis WJ*. Bilateral murine tumour models for analysis of the cellular and molecular events associated with immune checkpoint blockade. Nature Protocols 2020 May;15(5):1628-1648. (*Corresponding authors)
- Rwandamuriye FX, Weston BJ, Lesterhuis WJ*, Zemek RM*. A Mouse Model of Incompletely Resected Soft Tissue Sarcoma for Testing (Neo)adjuvant Therapies. Journal of Visualized Experiments 2020 Jul 28;(161). doi: 10.3791/60882. (*Corresponding authors)
- Zemek RM, Chin W, Millward MJ, Nowak AK, Lake R, Lesterhuis WJ. Sensitizing the Tumor Microenvironment to Immune Checkpoint Therapy. Frontiers Immunology 2020 Feb 18;11:223. doi: 10.3389/fimmu.2020.00223.
- Zemek RM, De Jong E, Chin W, Fear F, Forbes C, Casey T, Hope D, Boon L, Forrest AR, O Muiri D, Millward MJ, Nowak AK, Lassman T, Bosco A, Lake R, Lesterhuis WJ. Sensitization to immune checkpoint blockade through activation of a STAT1/NK axis in the tumor microenvironment. Science Translational Medicine 11 (501), eaav7816, 2019.
- Chin WL, Zemek RM, Lesterhuis WJ, Lassmann T. Functional genomics in cancer immunotherapy: computational approaches for biomarker and drug discovery. Molecular Systems Design & Engineering, 2019.

Financial Statements

Year ended 30 June 2021

ABN: 42 030 465 053

CHILDREN'S
Leukaemia & Cancer Research
Foundation (INC.)

Suite 3/100 Hay Street
Subiaco WA 6008

PO Box 1118
West Perth WA 6872

PATRON - Justin Langer AM
ABN: 42 030 465 053

STATEMENT BY THE COMMITTEE OF MANAGEMENT

The Committee Members have determined that the Foundation is not a reporting entity, and that this special purpose financial report should be prepared in accordance with the accounting policies outlined in Note 1 to the financial report.

In the opinion of the Committee of Management, the accompanying financial reports:

1. (a) The financial statements and notes are in accordance with Part 5 of the Associations Incorporation Act 2015; and

   (b) The accompanying Operating Statement gives a true and fair view of the operating excess of the Foundation for the financial year; and

   (c) The accompanying Balance Sheet gives a true and fair view of the state of affairs of the Foundation as at the end of the financial year.

2. At the date of the statement there are reasonable grounds to believe that the Foundation will be able to pay its debts as and when they fall due.

This statement is made in accordance with a resolution of the Committee of Management and is signed by and on behalf of the Committee of Management by:

.....

Chief Executive Officer – Andrea Alexander

.....

Treasurer – Justin Bruce

Date: 09/11/2021

The accompanying notes form part of the financial statements.

+61 8 9363 7400 admin@childcancerresearch.com.au childcancerresearch.com.au

INDEPENDENT AUDIT REPORT

TO THE MEMBERS OF THE CHILDREN'S LEUKAEMIA & CANCER RESEARCH FOUNDATION (INC)

NICK DEL POPOLO
CHARTERED ACCOUNTANT
9 CARRINGTON STREET
NORTH PERTH, WA, 6006
Ph: 0419 922 776

9 November 2021

TO THE MEMBERS
THE CHILDREN'S LEUKAEMIA & CANCER RESEARCH FOUNDATION (INC)
We have audited the financial statements of Children's Leukaemia & Cancer Research Foundation (INC)(The Foundation) for the year ended 30 June 2021.

The Foundation's Management Committee are responsible for the preparation of the financial statements. We have conducted an independent audit of these financial statements in order to express an opinion on them to the members of the Foundation. The Management Committee's responsibility also includes such internal control as the Management Committee's determine necessary to enable the preparation of a financial report that gives a true and fair view and is free from material misstatement, whether due to fraud or error.

The audit has been conducted in accordance with Australian Auditing Standards to provide reasonable assurance as to whether the financial statements are free of material misstatement. Our procedures included examination, on a test basis, of evidence supporting the amounts and other disclosures in the financial statements, and the evaluation of accounting policies and significant accounting estimates. These procedures have been undertaken to form an opinion as to whether in all materials respects the financial statements are presented fairly in accordance with Australian Accounting Standards so as to present a view of the Foundation which is consistent with our understanding of its financial position and the results of its operations.

The financial statements include fundraising receipts. It has not been practicable to determine whether pledged monies from external fundraising activities have been received and banked through the Foundation's accounts.

The Audit opinion expressed in this report has been formed on the above basis.

INDEPENDENCE
In conducting our audit, we have complied with the independence requirements of the Australian professional ethical pronouncements.

AUDIT OPINION
In our opinion, the financial statements present fairly the financial position of Children's Leukaemia & Cancer Research Foundation (INC) as at 30 June 2021 and the results of its operations for the year ended 30 June 2021 in accordance with applicable Accounting Standards to the extent described in Note 1.
In addition;
a.The financial statements satisfy the requirements of Part 5 of the Associations Incorporation Act 2015;
b. We have been given all information, explanations and assistance necessary for the conduct of the Audit;
c. The Foundation has kept financial records sufficient to enable financial statements to be prepared and audited;
d. The Foundation has kept other records as required by Part 5 of the Associations Incorporation Act 2015

EMPHASIS OF MATTER- BASIS OF ACCOUNTING
We draw attention to Note 1 to the financial report, which describes the basis of accounting. As a result, the financial report may not be suitable for another purpose. Out audit opinion is not modified in respect of this matter.

Nick Del Popolo
Chartered Accountant
Registered Company Auditor

Liability limited by a scheme approved under professional standards legislation

AUDITORS INDEPENDENCE DELCLARATION

TO THE COMMITTEE OF MANAGEMENT OF THE CHILDREN'S LEUKAEMIA & CANCER RESEARCH FOUNDATION (INC)

I declare that, to be best of my knowledge and belief, during the year ended 30 June 2021 there have been no contraventions of:

i.Any applicable code of professional conduct in relation to the audit

Name of firm:	N DEL POPOLO
Name of partner:	N DEL POPOLO
Date:	1st July 2021
Address:	9 CARRINGTON STREET NORTH PERTH WA 6006

Nick Del Popolo
Chartered Accountant
Registered Company Auditor

Liability limited by a scheme approved under professional standards legislation

Operating Statement 01/07/2020 - 30/06/2021

Revenue	2020/2021	2019/2020
Subscriptions	$1,711	$2,990
Donations & Promotions	$148,934	$208,069
Community Activities	$139,236	$157,119
Raffles & Direct Mail Campaigns	$327,088	$513,787
Schools & Associations	$9,255	$9,020
Commercial Support		
Marketing Revenue	$250	-
Toolmart Australia	$6,815	$544
Triple Vend/Austway	$1,110	$250
United Fundraisers	-	$1,779
VLT	$968	$274
Woolworths Australia	$2,855	$3,656
Grants & Gifts in Wills		
Gifts in Wills	$133,266	$276,072
3BL (Brain Tumour Research Project)	$325	$315
Job Keeper Payments	$42,000	$36,000
ATO Cash Boost Payments	$27,070	$45,116
Interest Received	$43,156	$102,952
TOTAL REVENUE	**$884,039**	**$1,357,943**

Expenditure	2020/2021	2019/2020
Admin, Staff & Other Costs	$659,793	$498,788
Depreciation	$31,972	$32,421
Market Value M/Mment (unrealised)	$(10,547)	-
Raffles & Direct Mail Campaigns	$162,169	$304,411
Promotions & Events	$64,020	$110,588
Property Outgoings/Refurbishment	$40,616	$48,681
SUB-TOTAL	**$948,023**	**$994,889**

Appropriations	2020/2021	2019/2020
Research Funding/Grants July to June expenditure:		
Channel 7 Telethon Trust - July to Dec 2020	$500,000	-
PRO10111/20728 Block Grant - Jan to June 2021	$357,357	$817,365
PRO20514 Dr S Malinge - UR Kees Fellowship - Jan to June 2021	$150,194	$294,446
PRO21183 Program Manager for TKI Cancer Centre - Jan to June 2021	$55,746	$28,998
Unexpended from 2019/Adjustment	-	$(140,809)
SUB-TOTAL	**$1,063,297**	**$1,000,000**

EXCESS/(DEFICIT) TRANSFER TO ACCUMULATED FUNDS	**$(1,127,281)**	**$(636,946)**

The accompanying notes form part of the financial statements.

Balance Sheet 30/06/2021

Accumulated Funds	Notes	2020/2021	2019/2020
Balance as at 01/07/2020		$6,610,102	$7,247,048
Excess/(Deficit) from Operating Statement		$(1,127,281)	$(636,946)
TOTAL ACCUMULATED FUNDS		**$5,482,821**	**$6,610,102**

These Funds are represented by

Current Assets	Notes	2020/2021	2019/2020
Cash on hand		$100	$100
Cash at bank		$538,585	$276,640
Gaming Commission		$31,532	$31,995
Term Deposits		$3,299,496	$3,999,000
TOTAL CASH AVAILABLE		**$3,869,713**	**$4,307,735**
Pre-payment		-	$500,000
Other Debtors		-	$26,952
Trade Debtors		-	$2,079
Shares at Cost		$22,189	$18,925
Share Options - At Cost		-	-
Change in Market Value		$13,702	$3,155
TOTAL CURRENT ASSETS		**$3,905,604**	**$4,858,846**

Non-Current Assets		2020/2021	2019/2020
Property - Land & Buildings			
Property 100 Hay Street Subiaco	2	$886,630	$886,630
Capital Improvements		$121,626	$121,626
Less: Accum Deprecation		$(27,366)	$(18,244)
Provision for Diminution in Value		$(198,256)	$(198,256)
Provision for Depreciation		$(109,016)	$(86,850)
Computer Equipment at Cost		$13,370	$13,370
Less: Accum Deprecation		$(13,370)	$(12,686)
Collectables		$2,199	$2,199
Property - Vacant Land			
Property 26 Parnell Pde Bassendean	2	$572,928	$572,928
Property 28 Parnell Pde Bassendean	2	$553,588	$553,588
TOTAL NON-CURRENT ASSETS		**1,802,333**	**$1,834,305**
TOTAL ASSETS		**$5,707,937**	**$6,693,151**

Current Liabilities	2020/2021	2019/2020
Trade Creditors	$(152,990)	$(12,103)
Grants Received in Advance	$(35,000)	
Accrued/Sundry Creditors	-	-
Leave Liabilities	$(84,829)	$(67,230)
Provision for AL/LSL on-costs	$(10,279)	$(10,500)
Total Years Tax Liabilities	$57,982	$6,784
TOTAL LIABILITIES	**$(225,116)**	**$(83,049)**
NET ASSETS	**$5,482,821**	**$6,610,102**

The accompanying notes form part of the financial statements.

Statement of Cash Flows as at 30 June 2021

Cash Flows From Operating Activities	Notes	2020/2021	2019/2020
Receipts from:			
Subscriptions		$1,711	$2,990
Donations and Promotions		$148,934	$208,069
Community Activities		$139,236	$157,119
Raffles and Direct Mail Campaigns		$327,088	$486,911
School and Associations		$9,254	$9,020
Commercial support		$250	$6,503
Grants and Gifts in Wills		$274,361	$357,503
Interest		$43,620	$102,302
Payments to clients, suppliers, employees and for research grants		$(1,378,750)	$(2,002,904)
NET CASH USED IN OPERATING ACTIVITIES	**3**	**$(434,296)**	**$(672,487)**

Cash Flows From Investing Activities	2020/2021	2019/2020
Investment in Term Deposits	$(250,595)	$(1,139,856)
Payments for Property, Plant & Equipment	-	-
Withdrawal of Term Deposits	$950,000	$1,679,00
Acquisition of PPE	-	-
Investment in Shares	$(3,264)	-
NET CASH USED IN INVESTING ACTIVITIES	**$696,141**	**$539,144**
Net change in cash and cash equivalents	**$261,845**	**$(133,343)**
Cash and cash equivalents, beginning of year	$276,740	$410,083
Cash and cash equivalents, end of year	**$538,585**	**$276,740**

The accompanying notes form part of the financial statements.

NOTE 1 - Statement of Significant Accounting Policies

The significant accounting policies which have been adopted in the preparation of this financial report are:

BASIS OF PREPARATION

The Financial Report is a special purpose financial report, which has been prepared to meet the requirements of the Management Committee to provide information to the Children's Leukaemia & Cancer Research Foundation (Inc). The Foundation is not a reporting entity and is not obliged to adhere to the mandatory reporting requirements of the Australian Accounting Standards. Notwithstanding the special reporting status of the foundation, the Management Committee have, unless otherwise stated followed generally accepted accounting principles in accordance with Australian Accounting Standards. The accounts have been prepared on the basis of historical costs and do not take into account the changing value of money. The Accounting policies are consistent with those prepared in 2020.

TAXATION AND GST

Children's Leukaemia & Cancer Research Foundation (Inc) is an income tax exempt body.

The Net amount of Goods and Services Tax and GST recoverable from or payable to the Australian Taxation Office is included as a current asset or liability in the Balance Sheet.

Revenue, Expenses and Assets are recognised net of GST.

EMPLOYEE ENTITLEMENTS

The amounts expected to be paid to employees for their pro-rata entitlement to long service leave and annual leave are accrued annually at current pay rates.

NOTE 2 - Valuation of Non-Current Assets - Property

Hay Street, Subiaco was purchased on 02/09/2010 and is valued at market valuation. The Market Valuation is at 19/06/2015 and is prepared by an independent licensed property valuer. 26 and 28 Parnell Parade, Bassendean, were transferred to the Foundation on 17/09/2013 by a deceased estate. They are valued at Committee of Management valuation based upon a real estate agents Appraisal and Report dated 18/09/2012 and a second real estate agents drive-by valuation dated 08/11/2013.

NOTE 3 – Operating Cash Flow

Reconciliation of cash flows from operating activities with current year operating excess.

	2020/2021	2019/2020
Cash flows from operating activities		
Net deficit for the year	$(1,127,281)	$(636,946)
Non-cash flows in operating deficit		
Deprecation	$31,972	$32,421
Diminution in share investments	-	
Market value movements in share investment	$(10,547)	$(17,439)
Net (deficit)/surplus before working capital changes	$(1,105,856)	$(621,964)
Net changes in working capital:		
Change in trade and other receivables	$529,494	$(27,526)
Change in trade and other payables	$124,688	$1,597
Change in provisions	$17,378	$(24,594)
Net Cash From Operating activities	$(434,296)	$(672,487)

NOTE 4 – Post Balance Date Events

Non - Current Assets, Property - Vacant Land

28 Parnell Parade, Bassendean was sold on 30/09/2021 and was settled on 15/10/2021.

26 Parnell Parade, Bassendean was sold on 14/09/2021 and will settle on 12/11/2021.

Make a difference to the 1000 children and adolescents **(0-19)** diagnosed with childhood cancer every year in Australia.

CHILDREN'S LEUKAEMIA + CANCER RESEARCH FOUNDATION

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