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

ANNUAL REPORT

2015/ 2016

For over thirty years the Children's Leukaemia & Cancer Research Foundation (Inc.) has been raising funds for research into childhood cancers.

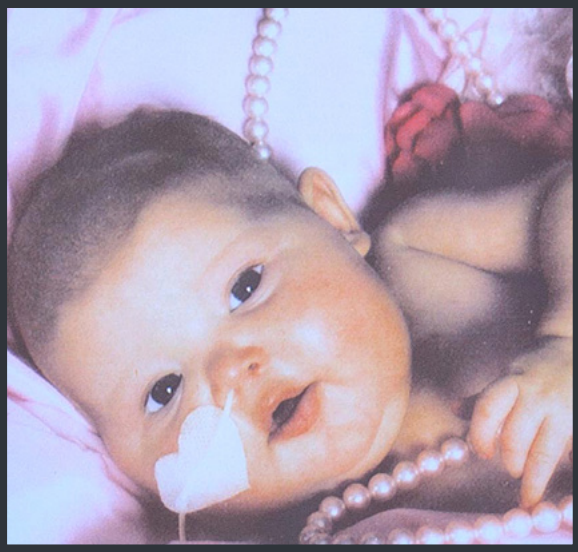
The Foundation relies on the generous support of the community to continue its vital research, as we do not receive State or Federal funding.

WHO ARE WE?

The creation of the Foundation was inspired by nine year old Jennifer Harper, who was diagnosed with leukaemia in 1977. When her father, Peter Harper, discovered that there was no research into children's leukaemia being done in Western Australia, he set out, together with other parents of children with cancer, to raise funds for this purpose. Sadly Jennifer passed away in 1978.

Australia has one of the highest incidences of childhood cancer worldwide. One in 500 Australian children will develop a cancer before 15 years of age – that's 600 Australian children diagnosed every year. Childhood cancer is the single greatest cause of death from disease in Australian children, with three children losing their lives to cancer every week. In Australia, childhood cancer is second only to breast cancer in terms of the number of years of life lost by the disease.

The quest to find cures for childhood cancer is one of medicine's greatest success stories. Fifty years ago only two percent of children with



cancer survived. Medical research alone has improved overall survival rates to 80 percent. With childhood cancer still the leading cause of death from disease in Australian children, there is more work to be done. There are still particular childhood cancers – such as brain tumours and neuroblastoma – with survival rates as low as 50 percent.

CLCRF has a commitment to ensure this ground-breaking research continues so that the future generations will be the ones to live cancer free. The Foundation relies on the generous support of the community to continue its vital research, as we do not receive State or Federal funding.

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Committee of Management

Mr Geoffrey CATTACH
(Chairman)

Mr Philip BRUCE
(Vice Chairman)

Mr Kim WILLIAMSON
(Treasurer)

Mr David CATTACH
(Secretary)

Mr Kimon ANDERSON

Mr Justin BRUCE

Professor Cathy COLE
(Nominee of Princess Margaret Hospital)

Professor Ursula KEES
(Nominee of Telethon Kids Institute)

Mr Michael PARKER

FOUNDER
Mr Peter HARPER

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

ADMINISTRATION STAFF
Mrs Andrea ALEXANDER
(Executive Officer)
Mrs Wendy KEARNS
(Executive Assistant)
Miss Katelyn LUSH
(Administrative Assistant)

Chairman's Report

It is with pleasure that I, once again, report to members on the operations of the Children's Leukaemia & Cancer Research Foundation (Inc.) for the year ended 30th June 2016.

As you all would be aware, last year's downturn in the economy has extended into our current year under review and the same trials and tribulations that plagued us in 2015 have continued into 2016.

On the brighter side, we have been able to maintain, and to some extent increase, research funding given our excellent accumulated fund position.

Finance:

For the year under review the Foundation suffered only its second loss in the past 36 years, this being $473,822 as compared with the 2015 loss of $807,269.

Notwithstanding the economic downturn, there are a number of contributing factors to this loss, however, I will allow the Treasurer to report specifically to the financial outcomes in his Report.

Needless to say, we haven't been sitting on our hands and have a number of strategies being put into place to ensure that we improve on our fundraising endeavours in the future.

Funding of Grants:

I am pleased to report that despite recent losses, our Foundation has been able to maintain the level of research funding during 2016, this being $999,908.70. A snapshot of the research grants currently being funded are as follows:-

(i) Triennial Block Grant 2015 - 2018
Titled Testing New Drugs for Infants with High Risk Leukaemia funding of $390,328

(ii) $1M Recognition of Excellence Funding Grant 2013 – 2017
Titled Molecular Genetics of Childhood Tumours funding of $121,839

(iii) CLCRF Fellowship Grant 2014 – 2016
Titled Targeting Therapy and Disease Outcomes in Paediatric Cancers funding of $201,621

(iv) Woolworths WA Research Fellowship 2013 – 2016
Titled Identifying the Molecular Abnormalities in Childhood Leukaemia funding of $108,757

(v) Midline Carcinoma Grant 2015 – 2017
Titled Effective Therapies for NUT Midline Carcinoma funding of $91,406

(vi) Morpholino Therapy for Cancer Grant 2015 – 2017
Titled The Molecular Genetic Landscape for Morpholino Therapies funding of $16,706

(vii) Co-funding Professor of Paediatric Research Grant 2015 – 2017
Funding of $26,364

(vii) Novel Therapies for Patients with Drug Resistant NUT Midline Carcinoma Funding of $42,889

It should be further noted that actual funding of research grants in 2016/17 will again be increased.

We are extremely grateful and accordingly extend our congratulations to Professor Ursula Kees and her dedicated team of researchers for their continued achievements both locally and internationally.

Telethon Kids Institute:

Once again we are proud to acknowledge the wonderfully cooperative working relationship we enjoy with the Telethon Kids Institute and, in particular, extend our thanks and appreciation to Professor Jonathon Carapetis, the Institute's Director, and Tim McInnis, Head of Development.

TELETHON KIDS INSTITUTE
Discover. Prevent. Cure.

Marketing Strategy & Development:

We have been very fortunate with the appointment of Kylie Dalton of Absolute Edge Media to create, manage and coordinate all of the Foundation's marketing, branding and promotion over the past three years.

Kylie has been instrumental in creating new income streams and in particular, the very successful innovative and creative "Dance for a Cure".

Accordingly I am pleased to announce that we have extended Absolute Edge Media's contract to 30/06/18 (which coincides with current block grant and admin funding) and look forward to the continued development of community and media relationships.

Community Activities:

Once again we are amazed at the wonderful and diverse support we receive from benefactors, businesses and the community at large.

Whilst such contributions will be individually acknowledged in our Executive Officer's Report, I would like to make particular mention of the wonderful contribution of the Rotary/Lions Bike Trek which this year raised the magnificent sum of $35,068 and since its inception in 2004 has raised a total of $644,000.

I congratulate members of our Community Fundraising Committee, under the chairmanship of Justin Bruce, who have worked cohesively with Kylie Dalton and our own Foundation staff together with the many volunteers who assisted in our fundraising endeavours.

I would also like to acknowledge that it is not just monies that are raised from these events but the awareness created which in turn initiates even greater support of our research endeavours.

Corporate Support Committee:

I would also like to commend our recently formed Corporate Support Committee under the Chairmanship of Kimon Anderson, who, with the support of Kirsten Pilatti, has undertaken the challenge of creating new income streams from the corporate sector, given our parlous financial outcomes of the past two years.

It is exciting to experience the evolution of the "Bench to Bedside" programme that is now up and running as well as the innovative and exciting "Board Room Series" designed to meet with 'captains of industry and commerce in order to create an awareness of our future research funding requirements.

It is sincerely hoped that the ultimate success of these strategies will be a definitive signpost to our future successes and financial viability.

Governance Issues:

I reported in last year's Annual Report that the Foundation was addressing governance issues, in particular, with regulations with the new ACNC Act (Australian Charities & Not for Profit Commission) and the drafting of a new Constitution which requires updating after 30 years and compliance with the ACNC.

It is pertinent to note that the purpose of the ACNC is to set out a minimum standard of governance and to promote public trust and confidence in registered charities.

To this end it is pleasing to report that we are in the last stages of finalising the 'draft' Constitution and are indebted to Allion Lawyers who have gratuitously undertaken to oversee the drafting of the new constitution and to ensure compliance with all statutory authorities. We are also indebted to R Sceales & Company who provided the necessary advice regarding compliance with Public Ancillary Fund guidelines.

As soon as timelines allow us to do so we will be calling an extraordinary general meeting in order to formally adopt the new constitution.

Patron:

We are extremely pleased that Justin Langer, our inaugural Patron, has, once again, agreed to continue in this role for the next appointment period of 2017.

We were extremely fortunate to have Justin accept the position of our first Patron and it is no surprise that he still holds this position. Notwithstanding his many commitments he has always given his support to the Foundation whenever called upon.

Ambassador:

Over the past 12 months, following on from a "strategic review" of the Foundation's operation's, we have undertaken to introduce a sub-committee environment. Accordingly we have an Executive Committee, a Finance Committee, a Corporate Support Committee, a Community Fundraising Committee and, finally an Alliances/JV's/Ambassadors/Patrons Committee. These sub-committees provide invaluable support to the Committee of Management.

I am also pleased to advise that, recently, Dr Ros Worthington OAM and radio personality, Lisa Fernandez, have accepted the role of Ambassadors to the Foundation.

Ros and Lisa join with our current Lord Mayor, Lisa Scaffidi, as CLCRF Ambassadors, who, together with our Patron, Justin Langer, help provide a public and community awareness of the Foundation. We are excited that our Ambassadors will support the Foundation in any way they can and help showcase the need for continued funding into childhood cancer research.

Foundation Staff:

As a Foundation we are blessed to have dedicated staff whose administrative efforts go far beyond a 9 to 5 environment.

To Andrea, Wendy and Katelyn I extend my personal appreciation for your passion towards the Foundation, your expertise and efficiency, plus outstanding loyalty, in your collective administrative roles.

Committee of Management:

I also wish to extend my appreciation to the dedicated and enterprising members of our Committee of Management who give freely of their time and provide outstanding business acumen.

One of the hallmarks of our committee over a long period of time has been stability however time does have its own influence notwithstanding restructuring arising out of our current constitutional review.

Accordingly, both through time constraints and constitutional restraints, we have accepted the resignations of three stalwarts in Valerie Stopp, Natalie Hiddlestone and John Vieira from the Committee of Management. All have given outstanding service and can be proud of their individual roles in what has been achieved by the Foundation. On the positive side, Valerie, Natalie and John will continue to support the Foundation by being involved in our sub-committees.

CONCLUSION

Our Foundation has now been in existence for 36 years, during this period of time we have raised approximately $30m, the research we have funded has made wonderful advances in the treatment of childhood cancers, our membership continues to grow and, best of all, we have been able to save young lives and give them the opportunity of a future.

To all of you, who have supported and contributed to this success, please accept our sincere thanks and grateful appreciation.

I wish everyone a very Merry Xmas and look forward to an exciting and challenging New Year.

Geoffrey R Cattach AM
CHAIRMAN **December 2016**

Executive Officer's Report

I am pleased to report to the Members of the Children's Leukaemia & Cancer Research Foundation (Inc) for the financial year 2015/2016.

Corporate Benefactors

Australian Industrial Supplies (AIS) 2015
Every year AIS hold a main event for their shareholders and supplier partners. In 2015 they chose CLCRF to be beneficiary. Board Member, Mike Parker, represented CLCRF at the function held in Adelaide in October 2015. Donations totalling $25,000 were received.
CLCRF were privileged to be selected as the beneficiary for the 2016 function, which was recently held in Melbourne and attended by Dr Mark Cruickshank.

Toolmart
We have been fortunate, over the past few years, to be one of two beneficiaries of funds from Toolmart's Tradie Expo, held annually at Ascot Race Course. During the 2016 weekend Foundation volunteers raised $6,183 from donations at the gate and a further $2,500 was donated from Toolmart.
Toolmart have also created a charity dollar scheme for their customers 'Toolmates Loyalty Program'. When certain items are purchased a portion of the sale is donated to the charity kitty. Funds from this program have been received in the 2016/2017 financial year.

Wellard Group
The Wellard Group continued to support the Foundation via the annual Christmas function and the Wellard 'Star of the West' Campdraft. Generous donation/s totalling $35,000 were received during the 2015/2016 period.

Benefactors

Deceased Estates:

Adamson Elizabeth – NSW	$	33,106
Costelloe Carmel – NSW	$	32,542
Edwards Ruth V – VIC	$	268,650
McIntosh Edna L – NSW	$	556
Napier Kath – WA	$	2,000
Westergaard Reginald – WA	$	20,000

The Foundation was not aware of some of these gifts until the benefactors had passed away.

Tate Family Foundation $28,500

This donation represents the fifth year of the Tate Family's commitment towards the $1M Recognition of Excellence grant.

Stan Perron Charitable Foundation $10,000

Mr Perron and his Foundation have been very loyal supporters of the Foundation since 1996.

Mr John Hughan $20,000

Mr Hughan has been a passionate supporter of CLCRF for many years.

To these individuals and organisations we extend our sincere thanks for their charitable support of the Foundation. There were many others who have provided support and financial assistance during 2015/2016. Their generosity is greatly appreciated. Donations of $500+ are listed elsewhere in this report.

2015 Dance For a Cure

This annual event was held in Forrest Place on November 8, 2015. Once again, hundreds of families from across WA united in a show of dance and pure joy to bring awareness of childhood cancer.

This event would not have been possible without the support from the City of Perth, Channel 9 Perth, Southern Cross Austereo, Seashells Hospitality Group and Perth Demons (for the use of Lathlain Oval for the rehearsals), not to mention all the smaller businesses that came on board to help with their donations.

The general public danced to Germonimo by Australian band Sheppard, who were very supportive of the event and licenced the song to CLCRF especially for the occasion.

A big thank you to our volunteer Dance For A Cure team who gave so generously of their time with meetings organising the dance and the two rehearsal days.

2016 Family Night Out

Our seventh family concert was held, in March, at a new venue – the Perth Zoo. Families had the opportunity of arriving early and touring the zoo before the concert commenced. The evening's entertainment was provided by the band Amanda Dee & Soothe.

We were also very fortunate to have access to the amazing 18 life-sized dinosaurs on display around the zoo.

Patrons enjoyed a gourmet BBQ and children also enjoyed the face painting, bubble machine and temporary tattoos.

The concert would not have been possible without support from the Perth Zoo, for the use of their beautiful facilities and Royal Life Saving Society (WA), who generously provided the first aid for this event. Much appreciation goes out to Awesome Balloon Creations (Mal & Judi) and our CLCRF volunteers.

The object of the family night out is to afford our members and supporters an event for a reasonable cost and to lift our profile within the community.

Despite there being a small loss on the concert, it was felt that the event was well worth the outcome of new supporters (near 85% new attendees) and a new relationship with the Perth Zoo. It is anticipated that the 2017 Family concert will see numbers grow!

Tele-Marketing Raffles

There were three raffles completed during the year ending June 2016. Revenue from these raffles totalled $319,541 which, after expenditure, resulted in a surplus of $124,148. Donations received via the raffles were included in the revenue figure.

Although the surplus figure was down compared with last year, it must be noted that there are many other charities now utilising this type of fundraising.
Our raffles continue to increase our profile in the community around Australia.
The Royal Life Saving Society WA (RLSSWA), through its call centres in Manjimup and Bridgetown, continue to undertake our telemarketing calls and the Hello Call Centre look after the administration of the raffle funds.

It should be noted, that these raffles are on a cost recovery basis and RLSSWA make NO profit from the services provided to the Foundation. We are extremely grateful to RLSSWA for their continued support of our cause; this relationship goes back well over 15 years to 2001.

Donation Appeal Campaigns

From each raffle campaign the Foundation has been able to establish a database of donors in addition to raffle supporters. Tax and Xmas donation appeals were sent to this donor database in 2015/16, as well as to a select number of donors from the Foundation database.

All four campaigns were successful and represent an effective complimentary fundraising program to the raffles. Net cash received from the campaigns was $111,499, which is higher than last year.

2015 South West Bike Trek

The Foundation's 12th South West Bike Trek kicked off in Mandurah on Monday the 12th October and finished in Augusta on Saturday the 17th. This year 30 cyclists took part in the 600 kilometre ride.

This event would not be possible without the support of the many service clubs, shires, companies and individuals. A total of $35,068 (this figure includes a $2,000 donation from AMP Services which was received in 2016/17 period) was raised from the trek.

Community Fundraising

During the 2015/16 period $157,620 was raised from community based activities.

The fundraising creativeness of Foundation supporters never ceases to amaze, from a Christmas Light display, proceeds from Crema Gourmet Coffee sales, donations from sales of BRAVE t-shirts, hoodies and sweatshirts from Popsicle & Co, the Toddle Waddle at Phoenix Shopping Centre, 6 year old Abraham selling his cupcakes, curry puffs and cereals to family and friends, the 'Silent Barista' who had his mouth taped closed for 2 mornings, school girls Ennika and DeriAnne Mak's crafty magnet sales - just to name a few!

One particular event that was held was 'Kate & Laura's Head Shave' - the Kate being our Administrative Assistant and Laura being Kate's friend. It was a very emotional moment to witness the dedication of Kate to carry through a commitment to shave her very long hair to raise funds for childhood cancer research. Unfortunately I lost the bet and had to shave mine as well! A BIG pat on the back to Kate and Laura because they raised $13,220.15! We are so very proud of them both.

Foundation Update

Two editions of the Foundation Update were published during the period under review. Thank you to Michele Seymour from Absolute Edge Media for her expertise in this area of graphic design.

Website

www.childcancerresearch.com.au

Our new website went live in June 2016, which was funded by a Lotterywest grant and a donation by Absolute Edge Media (AEM). It was designed and implemented by AEM as well.

I would like to sincerely thank Phil Solomon, of Bay Web Design (formerly Topshelf) of New Zealand, who, over the years had redesigned (twice) and maintained the old web site at no cost to the Foundation. Thank you Phil – your generosity and patience was endless.

It is worth noting that during the period under view over $19,000 was donated via the website.

Social Media

https://www.facebook.com/CLCRF

Currently CLCRF has 3,303 Facebook followers (83% women and 17% men) and provides a useful communication platform for engaging members/ supporters. The majority of followers, 2893, are from Australia.
Content of our page is varied, such as information about events, support/ donations received, items relevant to childhood cancer and humorous items.

https://www.facebook.com/flamealive

This page has now become our Dance For A Cure facebook page and has 2,612 likes. This page is used mainly to promote the Dance For A Cure and any other events that are planned.

https://twitter.com/CLCRF

We currently have 133 followers on Twitter. The Twitter account is mainly used when at events eg Dance For A Cure, Swan River Run, Family Night Out.
These social media platforms have proved to be of great benefit to the Foundation.

Membership

As at November, the Foundation has 608 current members. This is a loss of 28 members since last year. Whilst a few new members have signed up during the year under review, we will endeavour to increase this number by 2017.

Fund Raising Platforms

Support for the Foundation has continued to come from many people around the world. CLCRF's fundraising profile continues to be strong via the online fundraising entities such as Everyday Hero, Go Fundraise and My Cause.

Funds raised via these platforms totalled $48,495 during 2015/16. The Foundation now as an Everyday Hero Giving Hub built into the new website. This enables supporters to sign up directly with EDH and start raising funds for CLCRF.

School/College Support

The Foundation again received support from school children around Australia. Support was received from Bannister Creek PS, Beaumaris PS, Glencoe PS, Goomalling PS, West Greenwood PS and Westfield Park PS.

Particular mention must be made of Christ Church Grammar – Romsey House, who have supported the Foundation since the late 1980's. Over $5,715 was raised via three students embarking on a 24 hour Swimathon, as well as other fundraising activities.

CONCLUSION

This year has been a great year in a very challenging environment when it comes to charities. Whilst there has been a reduction in revenue we feel we have stayed strong with our relationships and started new ones in our community that we feel will be very beneficial in the future. Even though 2017 forecasts another difficult year for the NFP industry, we're on the right track to ride through it and come out with a good result.

In March 2016 Wendy and I attended the Fundraising Institute of Australia's international conference in Melbourne. For not-for-profit organisations, attendance at these conferences is essential to stay in touch with the industry and to network with peers. Thank you to the Committee for their support of this professional development.

A heartfelt thank you to my Executive Assistant, Wendy Kearns, and our Administrative Assistant, Katelyn Lush, for their tireless efforts, commitment and support during the past year.

Also to the team at Absolute Edge Media who go above and beyond for the Foundation.

Our Board of Management continue to provide me with support and guidance. It is an honour to work for such a dedicated group of people.

I would like to take this opportunity to wish everyone a very Merry Christmas and a safe and peaceful 2017.

Andrea Alexander
EXECUTIVE OFFICER
November 2016

CHILDREN'S LEUKAEMIA & CANCER RESEARCH 2015/2016

Funding: **Triennial Block Grant (2012 – 2015 and 2015 - 2018)**

Researcher: **Professor Ursula R Kees**

Title: **Testing New Drugs for Infants with High-Risk Leukaemia**

Leukaemias are cancers of the blood and are the most common cancer in children, particularly acute lymphoblastic leukaemia or ALL. Research over the past fifty years has led to massively improved cure rates. Around 90% of childhood and adolescent leukaemia patients can expect to be cured of their disease. In sharp contrast, newborns and children less than 12 months at diagnosis face a dismal outlook. Strikingly, in leukaemia patients less than 3 months at the time of diagnosis, the survival rate is only 30%. For this reason we call them high-risk leukaemias. In an attempt to find better therapy for these patients, international study groups have conducted many therapeutic studies, and the babies were given more intensive therapy. Unfortunately, this led to a large number of toxic deaths of patients, and did not improve overall survival. We urgently require novel therapies. Understanding the biology of this disease holds the key.

To study the biology we investigated the genetic features of the leukaemia cells from babies, and performed genetic analyses using state-of-the-art next generation sequencing technology. We gained novel insight into genes that are involved, their contribution to disease progression and resistance to chemotherapeutic drugs. We confirmed that a gene called MLL is not in its normal position on chromosome 11 where it normally is located, but chromosome 11 is broken at the site and fused to part of another chromosome. We know that such fusions that are only present in the leukaemia cells and not in the patient's normal cells, confer poor prognosis for the patient. We also found that infant patients inherited extremely rare versions in other genes that are known to play a role in cancer. Importantly, these molecular studies identified several known cancer-causing genes. This knowledge allows us to select modern drugs that target these altered genes to improve treatments of babies with leukaemia.

We used the leukaemia specimens from the patients to generate cell lines, so that the cells can be kept alive in the laboratory. These cell lines allow us to determine which drugs are effectively killing the leukaemia cells. We have generated a panel of nine cell lines and used the same methods to analyse their genetic features, as was done for the leukaemia cells from the patients. This confirmed that the cultured cells showed the identical fusions of the MLL gene as present in the leukaemia cells from the patients. We then screened the panel of cell lines against 150 approved cancer drugs, which is the first comprehensive assessment of the drug response in leukaemia cells from babies. The information obtained clearly showed that some of the currently used drugs are not very effective at killing the leukaemia cells in the test tube. However some of the novel drugs, e.g. Romidepsin, Carfilzomib and Dinaciclib were very effective, yet are not used in contemporary protocols for patients.

In order to determine whether these new drugs would be able to enhance the efficacy of currently used drugs we conducted a large screening experiment. We tested each of the three new drugs in combination with eight cytotoxic drugs that are currently used in treating babies with leukaemia. Of these 24 drug combinations, 12 showed enhanced killing of the leukaemia cells. Now we are extending these studies to cell lines from other patients. One of these successful drug combinations was further tested in our preclinical model system. We could demonstrate that this therapeutic approach effectively reduced the leukaemia burden in vivo – the drug combination was more powerful than each drug alone.

Our studies have identified new drug combinations that could be of benefit for babies with leukaemia. Our results have been presented to the international study group of the Children's Oncology Group, and our findings are intended to be integrated into future international clinical trials on infants with leukaemia.

These and other studies have generated a number of research publications and have allowed us to leverage additional funding to support the work. These details are provided below:

Additional Funding Leveraged:

- Telethon - Perth Children's Hospital Research Fund (2015-2017): Combinatorial Therapeutics In High-Risk Infant Acute Lymphoblastic Leukaemia (Kotecha RS, Kees UR, Cruickshank, MN, Lassmann T, $237,180)
- The Kid's Cancer Project Grant (2015): Improving the Treatment for Infants with Leukaemia (Kees UR, Cruickshank M, $115,000).
- The Kid's Cancer Project Grant (2014): Improving the Treatment for Infants with Leukaemia (Kees UR, Cruickshank, M, $100,000).
- NHMRC Project Grant ID1011499 (2011-2015): Targeting Drug-Resistance in Childhood Leukaemia (Kees UR, Lock RB, Beesley AH, $626,732).
- NHMRC Project Grant ID1007586 (2011-2014): The Role of Connective Tissue Growth Factor in The Pathobiology of Lymphoid Tumours and Response to Therapy (Kees, UR, Beesley AH, Charles AK, $601,732).

Recent Publications:

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Hooper CM, Hawes SM, **Kees UR**, Gottardo NG and Dallas PB, 2014. Gene expression analyses of the spatio-temporal relationships of human medulloblastoma subgroups during early human neurogenesis. PLoS ONE 9(11): e112909. doi:10.1371/ journal.pone. 0112909

Samuels AL, Heng JY, Beesley AH and **Kees UR**, 2013. Bioenergetic modulation overcomes glucocorticoid resistance in T-lineage acute lymphoblastic leukaemia. British Journal of Haematology, 2014. 165, 57-66.

Beesley AH, Stirnweiss A, Ferrari E, Endersby R, Howlett M, Failes TW, Arndt GM, Charles AK, Cole CH and **Kees UR**, 2013. Comparative drug screening in NUT midline carcinoma. British Journal of Cancer, 2014.110(5):1189-98.

Welch MD, Greene WG and **Kees UR**, 2013. Hypomethylation of the CTGF gene locus is a common feature of paediatric pre-B acute lymphoblastic leukaemia. British Journal of Haematology, 2013, 162(4):537-41

Beesley AH, Firth MJ, Anderson D, Samuels AL, Ford J and **Kees UR**, 2013. Drug-gene modeling in pediatric T-cell acute lymphoblastic leukemia highlights importance of 6-mercaptopurine for outcome. Cancer Research, 2013, 73(9):2749-59.

Thompson-Wicking K, Francis RW, Stirnweiss A, Ferrari E, Welch MD, Baker E, Murch AR, Gout AM, Carter KW, Charles AK, Phillips MB, **Kees UR** and Beesley AH. Novel BRD4-NUT fusion isoforms increase the pathogenic complexity in NUT midline carcinoma. Oncogene, 2013, 32(39):4664-74.

Tesfai Y, Ford J, Carter KW, Firth MJ, O'Leary RA, Gottardo NG, Cole C and **Kees UR**. Interactions between acute lymphoblastic leukemia and bone marrow stromal cells influence response to therapy. Leukemia Research 2012, 36: 299-306.

Kotecha RS, Ford J, Beesley AH, Anderson D, Cole CH and **Kees UR**, 2012. 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):1447-50.

Francis RW, Thompson-Wicking K, Carter KW, Anderson D, **Kees UR** and Beesley AH, 2012. FusionFinder: a software tool to identify expressed gene fusion candidates from RNA-Seq data. PLoS One 2012, 7(6):e39987.

Funding: **Million Dollar Recognition Award (2012 – 2017)**
Researcher: **Professor Ursula R Kees**
Title: **Molecular Genetics of Childhood Tumours**

The most common cancer diagnosis in children and adolescents is leukaemia, in particular acute lymphoblastic leukaemia or ALL. More than 50 years ago a few clinicians pioneered the use of what we now call chemotherapy - drugs that are toxic and preferentially attack leukaemia cells. A tremendous international cooperation by clinicians and scientists identified drug combinations that can eliminate the ALL cells and cure the patients. Steady progress has pushed the cure rate in some childhood patients to 95%, yet close to 40% of deaths occur among patients who are expected to have a very good response to multi-drug therapy, and be cured. The burden of disease, calculated in "person years of life lost" due to disease, is 67 years for children with cancer, compared to 16 for breast cancer patients. Patients with leukaemia are treated with up to twelve different chemotherapeutic drugs. These regimens are very toxic to normal cells of the patients, and lead to short and long-term sequelae. Patients who survive childhood leukaemia suffer from these effects all their lives. Sadly, in some patients the disease comes back and the patients relapse. Most relapses of ALL occur in the bone marrow where the disease originates. At the time a patient is diagnosed, the bone marrow does not contain many normal cells, but instead is almost totally replaced by ALL cells. The cause of relapse is often due to the fact that the chemotherapeutic drugs are no longer toxic for the leukaemia cells - because they have changed their genetic features somewhat and as a result have become resistant. We have recently discovered that leukaemia cells use another escape method, and this is triggered by a response in the normal cells that surround them. This seems to be a slow process and takes place in the bone marrow. It ultimately leads to protection of leukaemia cells by the microenvironment.

We discovered that ALL cells have the capacity to influence their environment. Almost all of them show high levels of a gene called connective tissue growth factor, or CTGF for short. We found out that the ALL cells rapidly secrete CTGF such that cells in the vicinity receive a CTGF signal. This finding prompted us to determine whether the growth of the leukaemia cells is dependent on the co-operation with the surrounding cells. We established a model system that allows us to analyse such mechanisms in vivo. We studied the development of the leukaemia and found that the human disease is mirrored perfectly in our model

system, including the destruction of the bone. Importantly, this model recapitulates the human disease and clinical symptom of skeletal abnormalities in children with a diagnosis of ALL.
We investigated the development of the disease in our model system and monitored each population of the surrounding normal cells. We could show clearly that during the initial phases the leukaemia cells did not expand, however the environment was remodelled to facilitate the subsequent support of the cancerous growth. The combined reactions of the surrounding cells appear to trigger expansion of the leukaemia cells, and this happened very rapidly. Understanding the cascade of events opens up new avenues to interfere with the disease process and to design new therapeutic approaches. Our goal is to find inhibitors of these mechanisms to stop the development of leukaemia.

Recent Publications:

Wells JE, Howlett M, Halse HM, Heng J, Ford J, Cheung L, Samuels AL, Crook M, Charles AK, Cole CH and **Kees UR**, 2016. High expression of connective tissue growth factor accelerates dissemination of leukaemia. Oncogene 2016, 35(35):4591-600.

Kotecha RS, **Kees UR**, Cole CH and Gottardo NG, 2015. Rare childhood cancers - an increasing entity requiring the need for global consensus and collaboration. Cancer Medicine, 2015, 4(6): 819-824.

Longville BA, Anderson D, Welch MD, **Kees UR**, Greene WK, 2015. Aberrant expression of aldehyde dehydrogenase 1A (ALDH1A) subfamily genes in acute lymphoblastic leukaemia is a common feature of T-lineage tumours. British Journal of Haematology 2015, 168(2):246-57.

Welch MD, Howlett M, Halse HM, Greene WK, **Kees UR**, 2015. Novel CT domain-encoding splice forms of CTGF/CCN2 are expressed in B-lineage acute lymphoblastic leukaemia. Leukemia Research 2015, 39 (8): 913-920.

Wells JE, Howlett M, Cheung LC, **Kees UR**, 2015. The role of CCN family genes in haematological malignancies. Journal Cell Commun Signal. 2015 9, (3):267-278.

Wells JE, Howlett, M. Cole CH and **Kees UR**, 2015. Deregulated expression of connective tissue growth factor (CTGF/CCN2) is linked to poor outcome in human cancer. International Journal of Cancer, 2015, 137(3): 504-11.

Cheung LC, Strickland DH, Howlett M, Ford F, Charles AK, Lyons KM, Brigstock DR, Goldschmeding R, Cole CH, Alexander WS and **Kees UR**, 2013. Connective tissue growth factor is expressed in bone marrow stromal cells and promotes interleukin-7-dependent B lymphopoiesis. Haematologica, 2014, 99(7):1149-1156.

Samuels AL, Beesley AH, Yadav BD, Papa RA, Sutton R, Anderson D, Marshall GM, Cole CH, **Kees UR** and Lock RB, 2014. A pre-clinical model of resistance to induction therapy in pediatric acute lymphoblastic leukemia. Blood Cancer J, 2014 4, e232.

Samuels AL, Heng JY, Beesley AH and **Kees UR**, 2013. Bioenergetic modulation overcomes glucocorticoid resistance in T-lineage acute lymphoblastic leukaemia. British Journal of Haematology, 2014, 165, 57-66.

Welch MD, Greene WG and **Kees UR**, 2013. Hypomethylation of the CTGF gene locus is a common feature of paediatric pre-B acute lymphoblastic leukaemia. British Journal of Haematology, 2013, 162(4):537-41

Beesley AH, Firth MJ, Anderson D, Samuels AL, Ford J and **Kees UR**, 2013. Drug-gene modeling in pediatric T-cell acute lymphoblastic leukemia highlights importance of 6-mercaptopurine for outcome. Cancer Research, 2013, 73(9):2749-59.

Tesfai Y, Ford J, Carter KW, Firth MJ, O'Leary RA, Gottardo NG, Cole C and **Kees UR**. Interactions between acute lymphoblastic leukemia and bone marrow stromal cells influence response to therapy. Leukemia Research 2012, 36: 299-306.

Francis RW, Thompson-Wicking K, Carter KW, Anderson D, **Kees UR** and Beesley AH, 2012. FusionFinder: a software tool to identify expressed gene fusion candidates from RNA-Seq data. PLoS One 2012, 7(6):e39987.

Funding: **CLCRF Research Fellowship (2010 – 2013; 2013 – 2016)**
Researcher: **Associate Professor Alex H Beesley**
Title: **Targeting Therapy and Disease Outcomes in Paediatric Cancer**

Dr Beesley was employed within the CLCRF Laboratory in the Division of Cancer and Leukaemia Research from 2003, and was awarded the inaugural CLCRF Research Fellowship in July 2010. In 2013, Dr Beesley renewed his Fellowship, with the aim of conducting research into a rare type of cancer called NUT midline carcinoma (or NMC). This is a terribly aggressive cancer that can affect children of all ages, and there is currently no cure. Patients are treated with aggressive chemotherapy and surgery but survival is typically less than one year.

The first report of this rare disease was published by Professor Kees in 1991, and we continue to be one of very few laboratories in the world studying its biology. Thanks to the funding provided from the CLCRF, we have been able to obtain material from investigators and tumour banks around the world to generate a unique panel of NMC cell lines here in Perth. Using this comprehensive panel, we have tested for drugs that might be more effective at killing the cancer cells, and we have also sent the samples to have their entire genetic code analysed, the first time that this has been done for this disease. This information will provide a blueprint of what goes wrong in NMC cells and the types of drugs that might be best for treatment. Central to the success of these projects is the science of computational biology or 'bioinformatics', which is the use of high-performance computing to analyse the enormously complex data that is generated by modern biological research approaches.

During his Fellowships Dr Beesley co-wrote two successful NHMRC Project Grant applications together with Professor Kees and applied to the NHMRC for additional funding to support the NMC research program. In 2014 he played a significant role in assisting Dr Anja Stirnweiss, a key member of ongoing the NMC research team, with her successful Raine Priming Grant submission, which provided additional funding for the NMC project. He has published 12 journal articles during his Fellowship and has been responsible for presenting research from the laboratory to community groups and scientific audiences, both in Australia and overseas, acknowledging the support from the CLCRF at each opportunity.

In July 2016, after many years of dedicated service, Dr Beesley moved on from his formal research position at the Telethon Kids Institute, but continues to hold an Honorary Position to enable ongoing collaboration with the teams of the Cancer Division.

Findings from research conducted during Dr Beesley's Fellowship have been presented in the following scientific forums and community groups:

- Science on the Swan Conference 2016: Cutting Edge, Perth (2016)
- EMBL | Stanford Conference in Personalised Health, Heidelberg, Germany (2015).
- Paediatric Pathology Society and Australia and New Zealand Paediatric Pathology Group Joint Scientific Meeting, Perth, WA (2015)
- Australia & New Zealand Children's Oncology Group (ANZCHOG) Conference, Perth WA (2015)
- Combined Biological Sciences Meeting, Perth, WA (2015).
- The Lorne Genome Conference, Victoria (2015).
- •The Australian Society for Medical Research (ASMR) Annual Symposium (2014-2015).
- Telethon Kids Institute Cancer Forum Seminar Series (2015)
- The iVEC Supercomputing Annual Symposium, Perth, Western Australia (2014).
- EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, Barcelona, Spain (2014).
- The European Association for Cancer Research Conference, Cambridge, UK (2013)
- The 'Beyond the Genome' Conference, San Francisco, USA (2013).
- The American Society for Human Genetics, Boston, USA (2013).
- The Australian Society for Biochemistry and Molecular Biology (ASBMB) Annual Symposium, Fremantle, WA (2012, 2014).
- 4th New Directions in Leukaemia Research Conference, QLD (2012).
- New Directions in Child and Adolescent Health Symposium, Princess Margaret Hospital (2012).
- Children's Cancer Institute Australia (CCIA), Sydney (2012).
- The Lorne Cancer Conference, Victoria (2012, 2013).
- 28th Annual Genes & Cancer Meeting, Warwick, UK (2011).
- Keystone Symposium 'Omics Meets Cell Biology', Alpbach, Austria (2011).
- The Perth Cancer Club, WAIMR (2011).
- The Cancer Council WA Symposium, Perth, WA (2011 & 2013).
- The Lowy Symposium: Discovering Cancer Therapeutics, Sydney (2013).
- Rotary-Lions Club South West Bike Trek Fundraiser Dinner, Pinjarra (2012, 2013, 2014).

Together these studies have generated a number of important research publications and have allowed us to leverage additional funding to support the work:

Additional Funding Leveraged (2011 – 2016):

- Raine Priming Grant (2015-2016): Protein signaling networks in NUT Midline Carcinoma (CI: Stirnweiss; AIs Beesley AH, Kees UR, $180,000).
- CLCRF Project Grant (2014): 'Finding the Most Effective Therapies for Midline Carcinoma' (Beesley AH, $132,817 over 2 years)
- CLCRF Project Grant (2014): 'Morpholino Therapy for Childhood Cancer' (Beesley AH, $223,796 over 2 years)
- NHMRC Project Grant ID1011499 (2011-2015): Targeting drug-resistance in childhood leukaemia (Kees UR, Lock RB, Beesley AH, $626,732).
- NHMRC Project Grant ID1007586 (2011-2014): The role of connective tissue growth factor in the pathobiology of lymphoid tumours and response to therapy (Kees, UR, Beesley AH, Charles AK, $601,732).
- CLCRF Research Fellowship (2013): 'Targeting therapy and disease outcomes in NUT Midline Carcinoma' (Beesley AH, $557,167, over 3 years).
- CLCRF Research Fellowship (2010): 'Targeting therapy and disease outcomes in paediatric cancer' (Beesley AH, $374,441 over 3 years).

Publications A/Prof Beesley (2011 – 2016):

Stirnweiss A, Oommen J, Kees UR, Beesley AH. The biology of bromodomain inhibition in the prototypical disease of BRD4 mutation - NUT Carcinoma. Manuscript in Preparation.

Stirnweiss A, Oommen J, Kees UR, Beesley AH. The molecular-genetic landscape and treatment options for NUT Carcinoma, an aggressive and fatal disease. Manuscript in Preparation.

Carter T, Charles AK, Murch AR, Beesley AH, Kees UR. A retrospective review of NUT-midline carcinoma prevalence at a Western Australian Paediatric Hospital. Manuscript in Preparation.

Yadav BD, Samuels AL, Wells JE, Sutton R, Venn NC, Bendak K, Anderson D, Marshall GM, Cole CH, Kees UR, Lock RB, Beesley AH. Heterogeneity in Mechanisms of Emergent Resistance in Pediatric T-Cell Acute Lymphoblastic Leukemia. Accepted Oncotarget, July 2016.

Stirnweiss A, McCarthy K, Oommen J, Crook M, Hardy K, Kees UR, Wilton S, Anazodo A, Beesley AH. Novel BRD4-NUT fusion in an undifferentiated sinonasal tumor highlights alternative splicing as a contributing oncogenic factor in NUT midline carcinoma. Oncogenesis 2015 (Accepted Sep 2015).

Beesley AH*, Samuels AL*, Yadav BD*, Papa RA, Sutton R, Anderson D, Marshall GM, Cole CH, Kees UR, Lock RB. A pre-clinical model of resistance to induction therapy in pediatric acute lymphoblastic leukemia [*Joint first-authorship]. Blood Cancer J 2014, 4:e232.

Beesley AH, Stirnweiss A, Ferrari E, Endersby R, Howlett M, Failes TW, Arndt G, Charles AK, Cole CH and Kees UR. Comparative drug screening in NUT-midline carcinoma. Br J Cancer 2014, 110(5):1189-98.

Samuels AL, Heng J, Beesley AH, Kees UR. Bioenergetic modulation sensitises acute lymphoblastic leukaemia cells to glucocorticoids. Br J Haematol 2014, 165(1):57-66.

Beesley AH, Firth MJ, Anderson D, Samuels AL, Ford J, Kees UR. Drug-gene modeling in pediatric T-cell acute lymphoblastic leukemia highlights importance of 6-mercaptopurine for outcome. Cancer Res 2013, 73(9):2749-59.

Thompson-Wicking K, Francis RW, Stirnweiss A, Ferrari E, Welch MD, Baker E, Murch AR, Gout AM, Carter KW, Charles AK, Phillips MB, Kees UR, Beesley AH. Novel BRD4-NUT fusion isoforms increase the pathogenic complexity in NUT midline carcinoma. Oncogene 2013, 32(39):4664-74.

Francis RW, Thompson-Wicking K, Carter KW, Anderson D, Kees UR, Beesley AH (2012). FusionFinder: A tool to identify expressed gene fusion candidates from RNA-Seq data. PLoS One 7(6):e39987

Kotecha RS, Ford J, Beesley AH, Anderson D, Cole CH, Kees UR (2012). Molecular characterization of identical, novel MLL-EPS15 translocations and individual genomic copy number alterations in monozygotic infantwins with acute lymphoblastic leukemia. Haematologica. Sept97(9):1447-50.

Funding: **CLCRF Project Grant (Mar 2014 – Mar 2016)**
Researcher: **Associate Professor Alex H Beesley**
Title: **Morpholino Therapy for Childhood Cancer**

Patients with NUT midline carcinoma (NMC) share a common genetic feature, which is a specific rearrangement of the DNA within the cancer cell. Whilst this abnormality contributes to driving the disease, it also represents an Achilles heel because it can be used as a 'target' to design specific therapies i.e. drugs that attack the cancer cell but leave healthy cells alone. In 2014 & 2015 we worked with Prof Steve Wilton from Murdoch University to develop a novel therapy designed to target this genetic abnormality.

This approach uses drugs called 'morpholinos' that interfere with the way genes are expressed in the cell and Prof Wilton has successfully pioneered this approach as a genetic therapy in the field of muscular dystrophy. The use of these agents in our NMC lines revealed unexpected information about the ways in which the NMC gene can be expressed. Specifically, we managed to induce a new variant of the NMC gene that can be expressed under certain conditions. Remarkably, in a patient diagnosed in 2014 at Sydney's Children's Hospital we were able to confirm this variant as an independent clinical subtype. Tragically this patient, a teenage girl, passed away only three months after diagnosis, demonstrating the voracity of the disease. Working closely with her doctors we were able to generate a cell line from this patient's tumour with which to further study its biology, resulting in a joint publication that was accepted by the journal Oncogenesis in 2015.

With this discovery we now know that there are at least five distinct molecular subtypes of NMC, as defined by the structure of this particular genetic feature, and we also know that they respond differently to chemotherapy drugs. However, we do not yet understand the full biological significance of these different subtypes, nor what determines these drug sensitivities.

To unravel this question, we have recently sequenced the full genetic code of our NMC cell lines and patient specimens to identify the critical features driving the disease. The ongoing work in the laboratory has linked these findings with drug-sensitivity data to yield a comprehensive map of the molecular genetic landscape of NMC and the biological pathways that are the most promising as targets for future therapies.

Funding: **CLCRF Project Grant (2016)**

Researcher: **Dr Anja Stirnweiss**

Title: **Novel Therapies for Patients with Drug Resistant NUT Midline Carcinoma**

Rare cancers represent roughly 20% of all human cancers and are associated with worse survival than are so-called frequent tumours. Patients often experience delays to accurate diagnosis, inadequate treatments and fewer opportunities to participate in clinical trials. NUT midline carcinoma is one of those rare cancers with 200 people affected worldwide. Patients range from newborns to the elderly, but the disease is most often diagnosed in children and adolescents.

To date, there are no survivors, and better treatments for this devastating disease are desperately needed. One major focus of our research is thus to find effective therapies to improve the fatal outcome for NUT midline carcinoma patients.

In NUT midline carcinoma the patient's genetic material is incorrectly repaired, which joins two genes (called BRD4 and NUT) and creates a new hybrid gene that causes the cancer. Importantly, drugs that are specifically designed to block the function of BRD4 called iBETs, have recently been developed. Since this treatment is likely to be the standard treatment for NUT midline carcinoma patients in the future, we have analysed the effects of an iBET called JQ1 in two of our pre-clinical NMC mouse models. By monitoring disease progression in these mice we were able to show that the iBET treatment tripled the survival time. The acquired data is now forming the basis to benchmark the efficacy of other promising drug candidates.

Our data from the pre-clinical mouse models is very encouraging, however we also have evidence suggesting that resistance may limit the therapeutic benefit of iBETs. This has important clinical ramifications given that iBETs are currently assessed worldwide in 21 clinical trials for cancers such as leukaemia, brain tumours, aggressive breast cancers and NUT midline carcinoma.

In our laboratory we have used a unique collection of cells, obtained from NUT midline carcinoma patients, to identify drug-induced changes in gene expression. We then performed a correlation analysis to identify changes that

are unique to iBET-resistant cells. Network analysis, which assesses how those genes are functionally connected to each other, highlighted the oncogene FOS to be a central player of the gene network that is associated with drug resistance. Removal of this gene from the resistant cells showed that FOS is not a driver of resistance, but an ideal marker to predict if the cancer cells will respond to iBET treatment. Ultimately, assessment of FOS could be used in the clinic to predict which patients will benefit from iBET treatment.

Dr Stirnweiss also collaborated with Dr Bree Foley from the Tumour Inflammation Group at the Telethon Kids Institute to see if the patients own immune cells could be used to kill NUT midline cancer cells. Interestingly, we have shown that an immune cell type called 'Natural Killer Cells' is very potent in attacking NUT midline carcinoma cells.
The central question is now how this action could be promoted in patients to reduce their tumour burden and ultimately increase survival.

Manuscripts in preparation:

Stirnweiss A, Oommen J, Cole CH, Kees UR, Beesley AH. The Molecular-Genetic Landscape and Treatment Options for NUT Midline Carcinoma - An Aggressive and Fatal Disease. (Anticipated submission January 2017)

Stirnweiss A, Dholaria H, Oommen J, Hardy K, Kotecha RS*, Beesley AH*. Successful Treatment of a Pediatric Undifferentiated Carcinoma With Multimodal Therapy. [* Joint last-authorship]. (Anticipated submission January 2017)

McEvoy M, Oommen J, Cole CH, Kees UR, Beesley AH*, Stirnweiss A*. The Role of FOS in iBET-resistant NUT Midline Carcinoma. [* Joint last-authorship]. (Anticipated submission January 2017)

Funding: **Woolworths Research Fellowship (2012 – 2016)**

Researcher: **Dr Mark N Cruickshank**

Title: **Identifying Molecular Abnormalities in Childhood Leukaemia to Improve Treatment**

Dr Cruickshank was employed within the CLCRF Laboratory in the Division of Cancer and Leukaemia Research from September 2012-September 2016, during which he was recipient of the Woolworths CLCRF Research Fellowship. The Fellowship enabled Dr Cruickshank to conduct research aimed at (1) identifying novel drugs for the treatment of high-risk infant leukaemia patients and (2) genetic mechanisms underpinning disease. Dr Cruickshank has continued researching genetic determinants of paediatric leukaemia and drug resistance.

As part of his Fellowship, Dr Cruickshank was involved in experimental design, data analysis and manuscript preparation for projects on infant ALL and childhood ALL, detailed under the CLCRF Triennial Block Grant. The long-term vision of these research aims are towards detection of genetic biomarkers that are predictive of drug responses, thus empowering clinicians with new molecular prognostic tests and novel drugs to design personalised therapies to cure this disease.

While many types of childhood leukaemia have shown remarkable improvements in patient survival (now up to 95%) over the last twenty years, infant leukaemia remains challenging to treat, with low survival (~30%) of the very young patients and significant morbidity for survivors. Dr Cruickshank recently published findings together with a large collaborative group headed by Prof Ursula Kees, reporting the activity of novel anti-cancer drugs for this vulnerable group of leukaemia patients. The study tested over 150 novel drugs including FDA-approved cancer therapies and further investigated the most potent drugs combined with 2 key contemporary drugs used in the clinic.

This approach allowed us to demonstrate that some drug combinations are consistently effective in killing infant leukaemia cells, while other drug combinations interact adversely to reduce their efficacy in some patient leukaemia cells. We also demonstrated that the most potent drug combination worked effectively in animal models of the disease. These results have been presented to members of the Children's Oncology Group Infant ALL Committee by clinician-scientist team member Dr Rishi Kotecha, for consideration of therapies to be included in clinical trials.

Dr Cruickshank has continued to collaborate with Dr Rishi Kotecha and Prof Ursula Kees throughout 2016 on testing novel anti-cancer agents to treat infant ALL patients. Furthermore, Dr Cruickshank is embarking on a follow-up drug discovery project focusing on 22 "next-generation" small-molecule targeted inhibitors obtained from commercial partners GlaskoSmithKline (GSK).

Dr Cruickshank has performed detailed genetic characterisation of infant leukaemia utilising state-of-the-art genome-sequencing

technologies, providing comprehensive characterisation of DNA sequence differences unique to infant leukaemia patients. Indeed, the genetic cause of infant leukaemia still remains elusive even though these sequencing technologies have successfully identified many gene mutations driving paediatric and adult cancers.

In collaboration with the Computational Biology Unit, Systems Immunology Group and the CLCRF Laboratory, Dr Cruickshank has been testing the hypothesis that gene mutations inherited from both parents are necessary to drive disease, even though these gene mutations do not cause disease in each of the parents. Dr Cruickshank coordinated the sequencing of patient samples obtained from Princess Margaret Hospital for Children and has analysed this data integrated with a larger cohort published by St Jude Children's Hospital. The combined Perth/St Jude dataset is the largest collection of genome sequencing data for this high-risk sub-type ever assembled (n=43 patients). The prevalence of gene mutations in the study cohort was compared to a large cohort of healthy adults (n=60,706 individuals).

This approach allowed us to find genes with mutations in infant leukaemia patients that are well established as cancer predisposition risk genes and rarely show mutations in healthy adults. Remarkably, around one third of infants carry mutations in genes that cause hereditary cancer syndromes, notably Noonan syndrome genes (SOS1 and KRAS) and Lynch syndrome genes (MLH1 and MSH2). Furthermore, we found that in many cases, infant leukaemia cells express multiple defective genes that are known to underlie a variety of hereditary cancer syndromes. Altogether, these results have identified for the first time, gene mutations associated with infant leukaemia that could help explain why this cancer is so aggressive and difficult to treat.

The unique resources generated by the CLCRF laboratory, including cell lines, are now being used to determine if specific gene mutations in infant leukaemia patients causes altered drug response. We are focused on determining if these mutations alter drug-resistance to conventional therapies or indicate sensitivity to any novel drugs. Thus, in addition to identifying novel gene defects associated with infant leukaemia in patients, we have characterized cell lines from these same patients to show that leukaemia cells can be grown in test tubes and carry the same genetic information as the original patient samples. These studies pave the way to test the efficacy of novel drugs on leukaemia cells with the mutations we have discovered. Dr Cruickshank has successfully secured funding from the Telethon Kids Institute "Blue Sky Research Grant" scheme to identify novel drugs targeting these mutations. Successful completion of this project will represent a major step towards further personalising care for leukaemia patients.

The combined Perth/St Jude dataset of 43 infant ALL patient samples provides the statistical power to contrast the unique features of very young patients diagnosed with leukaemia at age less than 90 days (19/43 patients). These very young patients have a significantly worse prognosis, however the underlying biology is unexplained. Our analysis of gene-expression in these leukaemia samples suggests that very young patients (diagnosed less than 90 days age) lack immune cells infiltrating the leukaemia specimen, while in contrast, cells of the immune system could be detected in older infant patients (diagnosed later than 90 days age). These results could point to differences in the immune system of newborns, and this is currently under further investigation in collaboration with Dr Rishi Kotecha and researchers within Systems Immunology, Tumour Immunology, Computational Biology teams at Telethon Kids Institute.

Dr Cruickshank has been collaborating with Telethon Kids Institute Tumour Immunology Group Leader, Dr Jason Waithman, with the aim of testing how the bodies' immune cells can be harnessed to fight cancer. Thus far we have developed methods that allow us to examine immune cells in test tubes by treating them with drugs and determining if treated immune cells show improved abilities to fight cancer.

In addition to this work, we have been testing ways to alter the cancer cell so that it is more visible to the immune system. This project aims to increase the expression of mutated genes that can be recognised by the immune system. We are focusing on the activity of EMA-drugs provided by GSK because these specific types of drug are known to function by activating gene expression. These projects have been funded by awards from the Telethon Kids Institute Precision Medicine Working Group (2015) and a "Blue Sky Research Grant" (2014) awarded to Waithman and Cruickshank.

Dr Cruickshank has been participating in collaboration with A/Prof Paul Watt (Phylogica) and A/Prof Pilar Blancafort (Harry Perkins Research Institute) investigating a novel targeted drug which functions by inhibiting a protein called MYC which is a commonly deregulated cancer-driver. This protein is frequently expressed at very high levels in childhood and adult cancers. There are presently no known targeted drugs capable of blocking activity of MYC.

Our research has clearly shown that a lead compound developed by Phylogica and tested in the laboratory of A/Prof Blancafort shows potent anti-MYC activity.

Dr Cruickshank has presented research from the Laboratory to community and scientific audiences in Australia, acknowledging the support from the CLCRF at each opportunity.

Findings from research conducted during Dr Cruickshank's appointments have been presented in the following scientific forums and community groups:

- South Australian Health and Medical Research Institute (2016)
- Australian Industrial Supplies Charity Auction (2016)
- CLCRF Fund-Raising Donor Meetings (2016)
- Telethon Kids Institute Fund-Raising Donor Meetings (2016)
- Telethon Kids Cancer Centre Reference Group Meetings (2016)
- New Directions in Leukaemia Research Conference (2016)
- WA Health Translational Network, Perth (2015)
- Telethon Kids Institute P4 Forum (2015)
- Telethon Kids Institute; Staff Retreat; Blue Sky Grant Presentation (2015)
- Australia & New Zealand Children's Oncology Group (ANZCHOG) Conference, Perth WA (2015)
- Telethon Kids Institute Children's Cancer Centre Forum (2015)
- Telethon Kids Institute; Discussion and Technical Seminar Series, Perth (2014)
- Children's Leukaemia & Cancer Research Foundation Meeting (2014)
- Australian Bioinformatics Conference (2014)
- The 'Beyond the Genome' Conference, San Francisco, USA (2013).
- The American Society for Human Genetics, Boston, USA (2013).
- Cancer Epigenomics Cell Symposium, Sites, Spain (2013)
- Telethon Institute for Child Health Research Seminar, Perth (2013)
- Perth Cancer Club, Perth (2013)
- Children's Leukaemia & Cancer Research Foundation Meeting (2013)
- Lorne Genome (2013)

Publications Dr Cruickshank (2012 – 2016):

Cruickshank MN*, J Ford*, LC Cheung, J Heng, S Singh, J Wells, TW Failes, GM Arndt, N Smithers, RK Prinjha, D Anderson, KW Carter, AM Gout, T Lassmann, J O'Reilly, CH Cole, RS Kotecha, UR Kees "Systematic chemical and molecular profiling of MLL-rearranged infant acute lymphoblastic leukemia reveals efficacy of Romidepsin". 2016 Leukemia, in press (doi: 10.1038/leu.2016.165).

Cruickshank MN, Dods J, Fenwick E, Karimi M, Rae A, Holers VM, Abraham LJ, Ulgiati D: Tandem E-box motifs control human Complement receptor 2 (CR2) promoter activity via RP58, E2A, USF proteins and localized chromatin accessibility. 2015 The International Journal of Biochemistry and Cell Biology 2015 Jul;64:107-19.

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Ursula R. Kees
Alex H Beesley
Mark N Cruickshank **25 November 2016**


CHILDREN'S
Leukaemia & Cancer Research
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DONATIONS $500 & ABOVE 2015/2016

Many generous people and organisations gave to the Foundation during July 2015 - June 2016. We have tried to make the following list as accurate as possible but please forgive us if we have omitted details of your gift. Space does not permit us to list the numerous other donations given.

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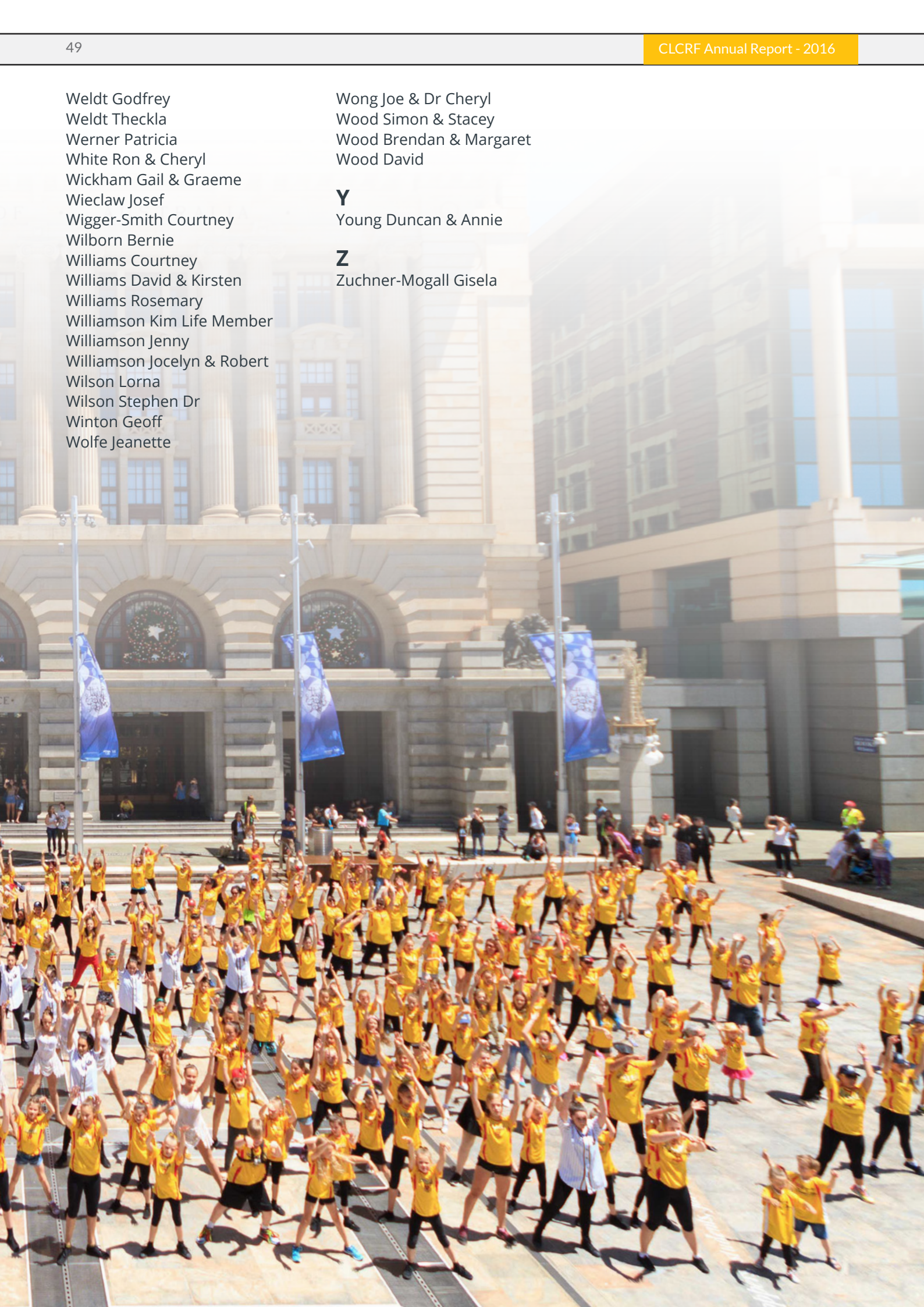

Children's Leukaemia & Cancer Research Foundation (Inc)

FINANCIAL STATEMENTS

Year Ended 30th June 2016

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

Suite 3/100 Hay Street
Subiaco WA 6008

PO Box 1118
West Perth WA 6872

Phone:
+61 8 9363 7400

Fax:
+61 8 9382 8798

admin@
childcancerresearch.com.au

childcancerresearch.com.au

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

The Trustee for Children's Leukaemia & Cancer Research Fund

ABN: 85 900 470 711

Patron: Justin Langer AM

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 accompanying Operating Statement gives a true and fair view of the surplus of the Foundation for the financial year; and

   (b) 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:

.....
Executive Officer – Andrea Alexander

.....
Treasurer – Kim Williamson

Date: 16/11/2016

The accompanying notes form part of the financial statements.

INDEPENDENT AUDIT REPORT

To: The Management Committee, Children's Leukaemia & Cancer Research Foundation (Inc)

SCOPE

We have audited the Financial Report for the Children's Leukaemia & Cancer Research Foundation (Inc) for the year ended 30 June 2016. The Management committee is responsible for the Financial Report.

Our audit has been conducted in accordance with Australian Accounting Standards. Our procedures include examination on a test basis, evidence supporting and other disclosures in the Financial Report. These procedures have been undertaken to form an opinion whether, in all material aspects, the Financial Report is fairly presented.

The audit opinion expressed in the 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 announcements.

QUALIFICATION

As is common with organizations of this type, it is not practical for Children's Leukaemia & Cancer Research Foundation (Inc) to maintain an effective system of internal control over donations and other fund raising activities until their entry in the Accounting Records. Accordingly our audit in relation to fund raising was limited to the amount recorded.

QUALIFIED AUDIT OPINION

In our opinion, except for the effect of such adjustments, if any as might have been determined necessary had the limitation discussed in the qualification paragraph not existed, the Financial Report presents fairly and in accordance with applicable Accounting Standards, the financial position of Children's Leukaemia & Cancer Research Foundation (Inc) at 30 June 2016.

AUDITOR

Signature _____

Full Name **Nick Del Popolo, ACA**
Address **9 Carrington Street, North Perth, WA, 6006**
Phone **0419 922 776**

Date 16.11.2016

Liability limited by a scheme approved under professional standards legislation.

OPERATING STATEMENT 01/07/15 - 30/06/16

REVENUE	2015/2016	2014/2015
Subscriptions	$ 1,406	$ 7,212
Donations & Promotions	$ 211,251	$ 150,274
Community Activities	$ 157,620	$ 292,394
Raffles & Direct Mail Campaigns	$ 432,122	$ 518,731
Schools & Associations	$ 10,123	$ 12,789
Commercial Support:		
Triple Vend/Austway	$ 1,220	$ 3,099
United Fundraisers	$ 1,908	$ 1,361
VLT	$ 1,923	$ 1,691
Grants & Bequests:		
Bequests	$ 356,794	$ 16,127
3BL (Brain Tumour Research Project)	$ 400	$ 9,671
Interest Received	$ 123,432	$ 231,018
TOTAL REVENUE	**$ 1,298,199**	**$ 1,244,367**
EXPENDITURE		
Admin/Salaries & Other Costs	$ 433,791	$ 561,132
Raffles & Direct Mail Campaigns	$ 197,393	$ 279,892
Promotions & Events	$ 100,827	$ 169,947
Block Grant Funding/Grants:		
Block Grant Allocation	$ 390,328	$ 423,792
1Mio Grant of Excellence	$ 121,328	$ 121,517
CLCRF Fellowship	$ 201,621	$ 178,112
Woolworths Fellowship	$ 108,757	$ 108,940
Midline Carcinoma Grant	$ 91,406	$ 102,020
Morpholino Therapy for Cancer Grant	$ 16,706	$ 67,544
CLCRF CRT Professor	$ 26,364	$ -
Novel Therapies NUT Midline	$ 42,889	$ -
Property Outgoings/Refurbishment	$ 30,100	$ 38,740
TOTAL EXPENDITURE	**$ 1,772,021**	**$ 2,051,636**
EXCESS/(DEFICIT) TRANSFER TO ACCUMULATED FUNDS	**$ (473,822)**	**$ (807,269)**

The accompanying notes form part of the financial statements.

BALANCE SHEET - 30/06/2016

ACCUMULATED FUNDS	2015/2016	2014/2015
Balance as at 01/07/2015	$ 7,438,991	$ 8,246,260
Excess/(Deficit) from Operating Statement	$ (473,822)	$ (807,269)
TOTAL ACCUMULATED FUNDS	**$ 6,965,169**	**$ 7,438,991**

These Funds are represented by:

CURRENT ASSETS:	2015/2016	2014/2015
Cash on Hand	$ 100	$ 100
Cash At Bank	$ 388,542	$ 1,401,057
Gaming Commission	$ 47,336	$ 46,254
Term Deposits	$ 4,771,354	$ 4,142,106
TOTAL CASH AVAILABLE	$ 5,207,332	$ 5,589,318
Trade Debtors	$ -	$ 4,000
Shares - At Cost	$ 17,166	$17,166
Share Options - At Cost	$ 1	$ 1
Provision for Diminution in Value	$ (15,566)	$ (12,366)
TOTAL CURRENT ASSETS	$ 5,208,933	$ 5,598,318
NON-CURRENT ASSETS:	2015/2016	2014/2015
Property Land & Buildings		
100 Hay St Subiaco	$ 886,630	$ 886,630
Capital Improvements - Subiaco	$ 121,626	$ 121,626
Provision for Diminution in Value	$ (198,256)	$ (198,256)
Provision for Depreciation	$ (16,200)	$ -
Computer Equiment At Cost	$ 7,182	$ 7,183
Property - Vacant Land		
26 Parnell Pde Bassendean	$ 572,928	$ 572,928
28 Parnell Pde Bassendean	$ 553,588	$ 553,588
TOTAL NON-CURRENT ASSETS	$ 1,927,499	$ 1,943,699
TOTAL ASSETS	**$ 7,136,431**	**$ 7,542,017**
CURRENT LIABILITIES	2015/2016	2014/2015
Trade Creditors	$ (119,031)	$ (2,873)
Accrued/Sundry Creditors	$ (5,252)	$ (73,114)
Leave Liabilities	$ (77,559)	$ (65,380)
Provision for AL/LSL on-costs	$ (6,800)	$ (6,800)
Total Years Tax Liabilities	$ 37,379	$ 45,141
TOTAL LIABILITIES	**$ (171,263)**	**$ (103,026)**
TOTAL ASSETS/LIABILITIES	**$ 6,965,169**	**$ 7,438,991**

The accompanying notes form part of the financial statements.

CHILDREN'S LEUKAEMIA & CANCER RESEARCH FOUNDATION (Inc)

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. Not withstanding 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 or fair value of non-current assets. The Accounting policies are consistent with those prepared in 2015.

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 19/06/15 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.

CONTACT US

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