From research to PRECISION MEDICINE

2015 Children's Medical Research Institute Annual Report
Childhood diseases are often invisible.

Children with cancer or a genetic disease experience a different kind of normal.

Sometimes that means living in hospital for months or years, or living a lifetime with a disability ... if they survive.

**Birth defects, cancer and genetic diseases are the leading causes of death in children under 14.**

Not every kid has a chance at a healthy future, but that's why CMRI is here.

Together, we can beat childhood diseases.
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Children's Medical Research Institute (CMRI) was Australia’s first dedicated paediatric medical research facility and has been working to create a healthier, brighter future for children for over 58 years. We passionately believe that, together, we can beat childhood diseases.

Our earliest successes included improved care for premature infants, introduction of rubella vaccinations, and microsurgery. These advancements saved lives. Now the most deadly conditions affecting children are birth defects, genetic diseases and cancer—they too need to be defeated.

We have internationally recognised teams of researchers who lead the world in the areas of embryology (birth defects), gene therapy (genetic diseases), neurobiology (epilepsy), and cancer who are working to find solutions. The dedication of our scientists is crucial, but so is the dedication of our supporters.

We need to work together to beat childhood diseases. The tireless efforts of our fundraising committees and the generosity of donors all over Australia are essential if we are to find ways to save more children’s lives. Participating in events like Great Cycle Challenge™, Ks for Kids®, or Jeans for Genes® Day can be fun as well as provide vital funds for research. Perhaps the most effective way to help is through regular giving, which provides reliable support for research programs that cannot simply be started and stopped depending on the availability of funds. Long-term, consistent effort is the key to success in any endeavour, and it’s true for finding cures for childhood diseases.

In these pages, you will learn more about our unique research and what we are doing to beat childhood diseases, as well as how people like you are providing the support needed to help us reach our shared goals.

Our Goals

→ Expand our research space and facilities to accelerate the search for cures
→ Revolutionise cancer diagnosis and treatment within 7 years
→ Deliver gene therapy cures for rare genetic diseases in children
→ See that our epilepsy treatments help children (and adults) around the world
→ Develop new cures for kidney disease and for infectious diseases
→ Find new and better treatments for most types of cancer

Welcome to our annual report for the calendar year, January through December, 2015.
Highlights

From basic research to precision medicine - 2015 was a transformative year for CMRI.

2015 Achievements

We regularly measure our achievements by the quality and impact of our research programs. 2015 was a year for major discoveries in each of our four core areas of research:

Cancer

→ Won the Australian Cancer Research Foundation anniversary grant for the nation’s most game-changing idea to fight cancer: this gave birth to ProCan™, and the international leaders in proteomics technology, Sciex, named CMRI a ‘Centre of Innovation in Precision Medicine’

→ Launched the ACRF Telomere Analysis Centre (ATAC), the first of its kind in Australia. With a range of advanced microscopes, the facility will help us better understand how cancer cells grow and what their weaknesses are

→ Many of our telomere research advances were published in world-leading scientific journals: Nature, Cell Reports, and Nature Reports

→ Uncovered the mechanism by which certain commonly occurring genetic risk factors – certain variations in the hTERT gene – predispose to cancer

→ Improved our understanding of how the telomerase protein, important for 85% of all cancers, interacts with DNA structures, called G-quadruplexes, as well as how it is recruited to telomeres, with implications for how anti-cancer therapies directed against telomerase should be developed in future

→ Investigated the mechanism by which the chemical, CMPD1, can kill neuroblastoma cancer cells

Gene Therapy

→ Conducted more detailed studies of how AAV, a vehicle for gene therapy, affects liver cells

→ Showed it is possible to inhibit liver fibrosis with gene therapy

→ Gene therapy advances developed at CMRI have culminated in a UK Medical Research Council Development Grant with the goal of clinical trials for metabolic liver disease treatment

Embryology

→ Identified a new disease gene, SIPA1L3, and uncovered how mutations in this gene cause eye defects

→ Developed a method for reducing the use of animals when studying how errors in genes cause diseases or birth defects

Neurobiology

→ Showed how disruption of the gene, senataxin, disrupts proteins, providing greater insight into its critical role in gene regulation to protect against neurodegeneration

→ Work showing MAP6 protein mediates neuronal connectivity was published in Nature Communications

→ Organised the International Chemical Proteomics Symposium, bringing researchers from North and South America, Europe and Asia to Westmead

General

→ Stage 1 building named best in its class by Master Builders Australia Awards 2015

→ CMRI won two Western Sydney Awards for Business Excellence – ‘Marketing’ and ‘Business of the Year’
CMRI conducts fundamentally important research that can lead to ground-breaking discoveries and pave the way for tomorrow’s treatments. We are extremely proud of what our research programs achieved in 2015.

One of our newest group Leaders, Dr Tony Cesare, had his research into telomeres and cancer featured on the cover of the international research journal Nature. He identified how one of the two key pathways preventing cancer formation – a process called ‘senescence’ – functions, and he was previously instrumental in showing how the other pathway ‘senescence’ works. These fundamentally important discoveries will have far-reaching implications for cancer research around the world.

Dr Cesare’s work was recognised at the inaugural CMRI Research Excellence Awards held in February, with honoured guests, Pru Goward, Minister for Medical Research, and Professor Tom Cech, Nobel Laureate in Chemistry, in attendance, together with philanthropist, Mr Xiangmo Huang, Chairman of the Research Excellence Foundation and his generous colleagues. Associate Professors Tracy Bryan and Robyn Jamieson were also recognised for their excellence in genetic research that has already had an impact on patients’ lives.

In total, CMRI researchers published nearly 50 articles in 2015, including many in high-profile international journals, such as Nature Communications, that will be read widely by the scientific community and significantly impact research progress globally.

The National Health and Medical Research Council (NHMRC) of Australia recognised the leading work of our scientists with a 37% grant success rate, double the national average. One application ranked in the top five in the nation. In addition, CMRI’s Professor Patrick Tam won two Australian Research Council top five in the nation. In addition, CMRI’s Professor Patrick Tam won two Australian Research Council Fellowships, the last four of which have been at the highest level (Senior Principal Research Fellow). Finally, Professors Patrick Tam and Ian Alexander were both elected as Fellows of the new Australian Academy of Health and Medical Sciences this year. 2015 showed that CMRI is not only leading the way in Australian research but on the world stage as well, especially in research innovation for precision medicine.

In December 2015, the Australian Cancer Research Foundation awarded CMRI its 30th Anniversary grant, a one-off prize of $10 million to support the most ambitious and potentially far-reaching cancer research idea in Australia. This award marked CMRI to be ‘the best of the best’, and has galvanized work that will soon revolutionise cancer diagnosis and guide how the best treatment is chosen, as well as open up new avenues for research into previously unimaginable cures. You can read more about this idea, ProCan™, in the pages of this annual report.

As a result of this success, CMRI was named a ‘Sciex Centre of Innovation in Precision Medicine’ and the first ever industrialized proteomics facility in the world. Sciex is a leading commercial producer of mass spectrometry technology. CMRI is partnering with researchers in Zurich, and elsewhere around the world, to make ProCan™ a reality.

Our many national and international scientific collaborators and partner institutions are all crucial to the work we do. The University of Sydney, our other Westmead Research Hub partners (The Children’s Hospital at Westmead, Westmead Hospital, The Westmead Institute for Medical Research, and the Institute for Clinical Pathology and Medical Research), and our paediatric research partners (Sydney Children’s Hospital Network and Children’s Cancer Institute)—these networks are helping us reach our research goals faster. In 2015, CMRI was a founding member of the Sydney Health Partners consortium, recognised by the NHMRC as an Advanced Health and Research Translation Centre. CMRI also became a member of the new Australian Genome Health Alliance.

In order to build on ProCan and to continue developing the facilities and resources that will ensure that our discoveries increasingly make a difference to the lives of children, we need to move on to Stage 2 of our building redevelopment as soon as possible. It continues to the focus for our fundraising efforts and special thanks goes to Board members, including Bruce Fink, Albert Wong, and Carolyn Forster, members of our Building Foundation Executive who are playing a leading role in this project.

We are also increasing our focus on fundraising that provides for the long-term support of research programs. We call our supporters who make a regular monthly gift ‘Game Changers’, because of the difference they are making to the future of children’s health.

The Jeans for Genes campaign saw its highest donations for several years in 2015, which is a great accomplishment for a 23-year-old campaign. New initiatives gave Jeans for Genes a fresh approach. The Great Cycle Challenge continues to record success. In total, over the last three years, supporters have cycled over 3 million kilometres and raised over $6 million for our cancer research programs.

As ever, we reserve a special thank you for our dedicated community-based Committees who donated their time, money and creativity in support of CMRI and have propelled Jeans for Genes and our other activities to such great success. We thank our hard-working researchers and other staff who carry out CMRI’s vital work every day. Thanks to our Board and those who serve on our Board Committees, including the Audit and Risk, Finance and Investment, Nominations and Remuneration, Intellectual Property and the Building Foundation. We farewell two, long-serving Board members, Mr Rodney Atfield, who is retiring from the Board after 16 years, and Prof Ian Caterson who served for 12 years. We thank them for their many valuable contributions to the Board and Committees over the years. We also welcome Mr Jeremy Waine to the Board, who will replace Mr Atfield as Treasurer, and also Mr James Wakim.

Finally, a very special thanks to all the children and family members who have shared their stories with us over the years. You can read some of these stories on our websites (cmri.org.au and jeansforgenes.org.au), in our mailings, and spontaneously shared on our Facebook and other social media pages. You will find some of their photos within these pages as well. There are countless more stories out there of brave individuals facing cancer and genetic disease, some succeeding in their fight and others not. It is for them that all of this—all of Children’s Medical Research Institute’s facilities, laboratories, researchers and supporters—exist. Our one goal is to create a brighter future for children and families like theirs.

Professors Frank Martin and Roger Reddel
May 2016
Report from the CFO

Not without its challenges, 2015 has nevertheless proven to be another year of successes for CMRI.

Our operating revenue has grown to $29 million (2014 - $25.6m) yielding an operating surplus of $3.4 million (2014 - $10.6m, including a building grant of $7.1m). The strong revenue performance included some growth in research grants income, but was mostly driven by increased fundraising through a major bequest from a deceased estate. Our investments income was adversely impacted by the decline in financial markets at year end, leaving us with a net investment gain for the year, but short of our annual target. Meanwhile, expenses were higher from the increase in staffing and building costs (including depreciation), stemming from the expanded building. Our total equity now stands at over $117 million and total assets over $125 million.

Having completed Stage 1 of our building expansion in 2014, we have quickly located several high-technology facilities into the new space. You will read in other sections of this report about the exciting developments with some of our new facilities: the ACRF Telomere Analysis Centre; the Vector and Genome Engineering Facility; and a relocated and expanded Biomedical Proteomics Facility. Cutting-edge science like ours relies on having cutting-edge equipment and information technology resources, and CMRI is proud of the investments it is making in these areas. These facilities will not only enhance the research work of our own scientists but will also be made available to other scientists in the Westmead Research Hub and surrounding Sydney metropolitan areas. There was great excitement at year-end when CMRI learnt it was the winner of the ACRF’s (Australian Cancer Research Foundation’s) 30th Anniversary Grant for $10 million of equipment. The resulting ProCan facility and project will be housed on the fifth floor of the Stage 1 tower and will be opened in 2016.

To pay for this expansion, we are investing in our fundraising programs, and we added two new campaigns in 2015 – Ks for Kids and FIT in Your Jeans for Genes. Our total fundraising costs were 31% of the related fundraising income (2014 – 32%), and of our total operating expenditure, 71 cents out of every dollar went to research services (2014 – 75 cents). Because of the fall in investments income and our increased operating costs generally, we could not cover our fundraising and administration costs from investments to the same extent as previous years. In 2015, approximately 70 cents of a fundraising dollar was effectively contributed to research (2014 – it was 97 cents). With current investment returns forecast to be at these levels for some years, a contribution rate of 70 cents in the fundraising dollar is a reasonable expectation for the future.

As ever, our income sources are diverse and, while individual performances may vary each year, the combination of returns is strong. High quality grant applications to government and private grant sources, public fundraising campaigns like Jeans for Genes and Great Cycle Challenge, a network of community fundraising committees, private philanthropy, commercialisation income derived from our Intellectual Property and a strategic allocation of investments, generating income for the long term, are all contributors to our overall success. We are fortunate not to be too reliant on any one factor, which will hold the Institute in good stead as it expands its research in the future.

Ralph Mitchell
Chief Financial Officer & Company Secretary
May 2016
## Financial Summary

### Profit and loss statement (in $ '000s)

<table>
<thead>
<tr>
<th></th>
<th>YTD Dec 2015</th>
<th>YTD Dec 2014</th>
</tr>
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<tbody>
<tr>
<td><strong>Revenues</strong></td>
<td></td>
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<td>Research</td>
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<td>Fundraising</td>
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<td>Investments</td>
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<td>Building redevelopment</td>
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<td><strong>Total</strong></td>
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<td><strong>Expenses</strong></td>
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<tr>
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<td>Fundraising</td>
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<td>Administration and facilities</td>
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<td><strong>Total</strong></td>
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<td>Surplus/(loss) before investment transactions</td>
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<td>Investment transactions, net and impairment</td>
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<tr>
<td>Surplus/(loss) from continuing operations</td>
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<td>Other comprehensive income from available-for-sale financial assets</td>
<td>(2,848)</td>
<td>(646)</td>
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<tr>
<td><strong>Total comprehensive income/(loss) for the period</strong></td>
<td>519</td>
<td>9,936</td>
</tr>
</tbody>
</table>

### Sources of Revenue, Income & Expenditure

#### Sources of Revenue (as per audited financial statements)

- **2015** – Total revenue: $29 million
  - 13% Investments*
  - 34% Grants for research
  - 52% Fundraising
  - 1% Building redevelopment

- **2014** – Total revenue: $33 million
  - 11% Investments*
  - 29% Grants for research
  - 37% Fundraising
  - 22% Building redevelopment

* Total Investments includes dividend distributions only

#### Sources of Income (excluding building redevelopment)

- **2015** – Total income: $29 million
  - 12% Total Investment Returns*
  - 35% Grants for research
  - 53% Fundraising

- **2014** – Total income: $28 million
  - 22% Total Investment Returns*
  - 34% Grants for research
  - 44% Fundraising

* Total Investment Returns include dividend distributions, investment transactions (profit/loss on redemption and impairment) and comprehensive income/loss on available-for-sale financial assets.

#### Sources of Expenditure

- **2015** – Total expenditure: $28 million
  - 71% Research
  - 17% Fundraising
  - 12% Administration and facilities

- **2014** – Total expenditure: $25 million
  - 75% Research
  - 16% Fundraising
  - 9% Administration and facilities

The above numbers have been extracted from the Audited Financial Statements of CMRI for the relevant periods. The full audited financial statements are available at cmri.org.au/About-Us/Annual-Reports-and-Financial-Statements.
Research Spend by Disease

2015 – Total research spend: $16 million

- Neurobiology 18%
- Genetics 19%
- Embryology 13%
- 50% Cancer

2014 – Total research spend: $15.4 million

- Neurobiology 18%
- Genetics 14%
- Embryology 18%
- 50% Cancer

Sources of Fundraising Income

2015 – Total fundraising income: $15 million

- 3% Trusts and Foundations
- 6% Other events and campaigns
- 14% Jeans for Genes®
- 17% Great Cycle Challenge
- 7% Direct Mail and Regular Giving
- 1% Building Redevelopment Donations
- 52% Bequests

2014 – Total fundraising income: $13 million

- 5% Trusts and Foundations
- 6% Other events and campaigns
- 19% Jeans for Genes®
- 17% Great Cycle Challenge
- 10% Direct Mail and Regular Giving
- 2% Building Redevelopment Donations
- 41% Bequests
1 in 20 children is born with a birth defect or genetic disease

There are over 6000 known genetic diseases

1 in 3 epileptics aren’t helped by current medication

Cancer is a leading cause of death in children under 14

CMRI researchers are facing these challenges head on. You’ll see that basic research (better called fundamental research) is a powerful approach to finding answers to a wide range of diseases.

In this section you’ll get to meet our research teams and learn more details about their important work.
The Cancer Research Unit investigates how cancer cells acquire the ability to multiply without limit – in other words, to become 'immortal'.

We are primarily focussing on the role played by telomeres, which are DNA sequences that act as protective caps at the ends of chromosomes, together with the other telomere research groups at CMRI (led by Tracy Bryan, Hilda Pickett and Tony Cesare) who work with us on various aspects of telomere function. Each time a normal cell divides, a small amount of telomere DNA is lost. This gradual telomere shortening functions as a ‘clock’ which counts down and ultimately stops normal cells from multiplying further.

Cancer cells evade this normal limit by adding back telomere DNA to overcome telomere shortening and thus become immortal. They do this using either an enzyme called telomerase or by using an Alternative Lengthening of Telomeres (ALT) mechanism. The overall aim of telomere research at CMRI is to find new cancer treatments that work by killing cancer cells that use either telomerase or ALT. The main emphasis of the Cancer Research Unit at present is on understanding ALT. Better understanding of this mechanism will enable us to develop better treatments against ALT cancers, which are some of the most aggressive types, including neuroblastomas, glioblastomas (brain tumours), osteosarcomas, and several types of soft tissue sarcomas.

2015 Research Achievements:

- Gained new understanding of how cancer cells switch on ALT. We showed that one of the normal functions of a gene (ATRX), which is very commonly found to be damaged in cancers that use ALT, is to keep ALT in check.
- Found that cancer cells which switch on ALT by losing ATRX gene function are much more fragile than normal cells when exposed to various forms of stress. We are using this knowledge to design treatments that will kill ALT-positive cancers with minimal side effects on normal cells.
- Worked with the other CMRI telomere groups on a range of projects including molecular details of ALT.
- Together with Dr Loretta Lau’s research group at The Children’s Hospital at Westmead, continued to study some childhood cancers that don’t have either telomerase or ALT. We will need to develop different treatment strategies for the relatively small group of patients who have this type of tumour.
- Identified a specific protein that helps cancer cells grow and spread throughout the body.

WHAT’S NEXT: develop methods of specifically killing ALT cells, and use the new ProCan™ facility to increase our understanding of both telomerase and ALT in cancers.

Telomeres are the protective structures at the ends of our chromosomes. They are made up of repetitive DNA that is lost each time a cell reproduces, but this DNA can be added back using either an enzyme called telomerase or a process called ALT.

Telomere length regulation involves an intricate balance between lengthening and shortening processes, which ultimately determines the capacity of a cell to divide. Telomere shortening is correlated with most types of cancer, while telomeres that are too short can cause aging and short telomere syndromes, characterised by bone marrow failure, organ failure or predisposition to rare types of cancer. We are currently investigating the ALT mechanism of telomere maintenance, and how this pathway can be targeted to treat cancers.

2015 Research Achievements:

- We identified the mechanism by which a common, cancer risk-associated allele in the telomerase reverse transcriptase locus results in an elevated risk of multiple cancers, including breast and ovarian carcinomas.
- We contributed to a study into heterochromatin formation at telomeres.
- We published a review on the mechanisms of activity and de-repression of the ALT pathway of telomere maintenance.
- We are developing novel techniques to characterise telomere DNA synthesis in ALT.
- We are establishing molecular screening platforms for ALT inhibitors.
- We are using bioinformatics to develop a machine learning algorithm that will allow computers to detect whether the DNA in a patient sample has short or long telomeres and whether a cancer uses ALT or telomerase. This will be important for personalised medicine approaches to cancer treatment.

WHAT’S NEXT: understand the mechanism of ALT-mediated telomere lengthening, and use these findings to develop new cancer treatments.
Cell Biology Unit

Unit Head: Associate Professor Tracy Bryan BSc (Hons) PhD

Diseases Impacted by Our Research:
→ 85% of cancers
→ Senescence (i.e. aging)
→ Bone marrow failure and other short telomere syndromes

Our research focuses on one of the major factors in at least 85% of all cancers affecting children and adults: the molecule telomerase. Cancer cells use telomerase to keep growing uncontrollably; thus telomerase is a key target for future cancer treatments, which are predicted to have fewer side effects than current radiation and chemotherapy.

We aim to understand the properties of telomerase in order to rationally design better anti-cancer treatments. This includes studying the association of telomerase with telomeric DNA, understanding how telomerase finds its way to the telomere, probing how the telomerase enzyme works and discovering its physical structure. In the long term, this knowledge will allow us to rationally design drugs against telomerase as potential anti-cancer therapeutics.

2015 Research Achievements:
→ We found that the TPP1 gene can cause a short telomere syndrome resulting in aplastic anaemia, a disease in which many patients die of bone marrow failure.
→ We began screening more patients with aplastic anaemia for mutations in TPP1 or other telomere-related genes, in order to determine the cause of their disease.
→ We have found many new proteins involved in bringing telomerase to the DNA, and thus we have many leads to investigate for inhibiting this process as a potential anti-cancer approach.
→ We have found that a special DNA structure at telomeres, called a G-quadruplex, can modify how telomere length is maintained (using ALT or Telomerase), which could be important for most cancers.
→ Through detailed study of the telomerase enzyme, we have a greater understanding of which parts of the protein are most important—except for one area, called the C-terminus, which we are currently investigating.
→ We determined a low-resolution structure of the telomerase enzyme, and we aim to have a higher resolution image of the structure in the near future. The clearer we can see the telomerase protein’s physical structure, the easier it will be to design potential anti-cancer drugs in future.

WHAT’S NEXT: gain a better understanding of telomerase structure to enable efficient anti-cancer drug design.

Cell Biology (image by Jonathan Arthur)

An interaction network generated during a search for the causative disease mutation in a patient with a form of congenital anaemia.
The Genome Integrity Group studies fundamental causes of cancer and aging. We seek to understand how our genome (the set of instructions guiding how our cells function) is protected, and when this protection fails, how a disease like cancer may result.

Children with mutations in genes important for genome health get cancers early in life and can develop rare syndromes. Much of our research focuses on telomeres, the protective caps at the ends of our chromosomes. We are studying how telomeres act normally during healthy aging to prevent cancer and how disruption in telomere function can result in changes to the genome that promote cancer. Recent work has centred on our discovery of intermediate-state telomeres. These are short ‘damaged’ telomeres that are protected by a protein called TRF2. Prior to this discovery of an intermediate state, it was thought that chromosome ends adopted either a protected or unprotected state. What we now surmise is that the unique properties of the intermediate-state are what protect against cancer, and we are working on understanding exactly how this protection is achieved.

2015 Research Achievements:

- In collaboration with the Salk Institute, we identified the mechanism of telomere-dependent cell death in aged, pre-cancerous cells. This was published in the top international journal Nature.
- We are studying how stress in the genomic DNA can activate telomere-specific mechanisms of cell death.
- We are using super-resolution microscopy to study how chromosome ends regulate cell growth arrest and cell death to establish a direct link from molecular changes at chromosome ends to cellular outcomes that impact cancer progression.

WHAT’S NEXT: We want to understand how some commonly used chemotherapeutic agents, and some new drugs that are in clinical trials, kill cancer cells through telomere-specific mechanisms.

Diseases Impacted by Our Research:

- Cancer
- Aging
- Short-telomere syndromes

Cell Cycle Unit

The Cell Cycle Unit studies normal cell division in order to understand what makes cancer cells grow out of control. We are also developing new anti-cancer treatments aimed at stopping cell division, especially in difficult to treat brain tumours, which are a leading cause of cancer-related deaths in young people.

We operate both a basic science research program and a translational drug discovery program. Despite the identification of many proteins involved in mitosis (the process by which cells divide and reproduce), the drivers of mitosis and how these proteins cooperate to complete mitosis is not fully understood. Cell division errors increase the potential of a cell becoming cancerous. Thus, understanding this basic biological process underpins our understanding of cancer, which can lead to the identification of targets for therapeutic anti-cancer drug design. We have already discovered that a subset of endocytic proteins are required for mitosis. Two of these (dynamin and clathrin) have been identified as anti-cancer drug targets, and these are the foundation of our drug development program, which is providing promising results.

2015 Research Achievements:

- We have implemented a technique called super-resolution microscopy, which has allowed us to study cell cycle proteins more closely than ever before—at the level of a single molecule. This has opened up entirely new ways of understanding cell division.
- We began building a super-resolution microscope for CMRI, rather than relying on borrowed equipment located elsewhere. This home-built microscope should be more cost effective and function better than commercially available microscopes, helping our research and the research programs of other labs across CMRI.
- The improved understanding we now have of mitotic proteins will help our drug development program to better refine the compounds that work best to inhibit cell division in cancer cells.
- We are currently focusing on drugs that inhibit the clathrin protein, but will return to studying dynamin-inhibitors once we have the results of their effectiveness in a breast cancer model.
- We already have a class of compounds, called PITSTOP, which we know inhibit clathrin. We have now developed a new class of drugs that bind clathrin differently. We believe these new drugs could have a synergistic effect with existing anti-mitotic drugs already in clinical trials. Clathrin drugs should be effective against all cancer types, but our research remains focused on the area of greatest need—brain cancer.

WHAT’S NEXT: continue to refine our lead compounds to find promising drugs that can one day be tested in clinical trials of brain cancer.

Diseases Impacted by Our Research:

- All cancers, especially...
- Glioblastoma brain cancers
Alex and his mum, Nerissa, share a rare genetic disease that affects their telomeres. It can cause bone marrow and other organ failure and gets progressively worse with each generation. Nerissa's brother died of the disease.

His mum said, "Alexander recently asked me what it would be like to be a normal kid? How do you answer that?"

The family are huge supporters of the telomere research happening at CMRI.

"The diagnosis was a total surprise for all of us; we are all shocked. But I feel very fortunate that it was recognised and that there is progress towards understanding it now.... Time is of the essence in treating this disease. I hope time is on our side."
The Cell Signalling Unit works to understand communication between nerve cells in the brain and between other cells in the body.

Our work focuses on understanding an important factor in signalling, a protein called 'dynamin' and it interacts with many other proteins involved in related roles inside cells. Basic research into how signals are sent between nerve cells and other cells in the body is underpinned by our application of mass spectrometry technology and drug discovery. We also are making developments in these technologies to inform further science advances. Our mass spectrometry technology allows analysis of phosphorylated proteins, key regulators in many biological processes, including nerve cell transmission. Our approach is called functional phosphoproteomics, where we use mass spectrometry and other tools to constantly learn more about how proteins become modified in seconds to control the fast activity in the synapses of nerve cells. Our ability to study phosphorylated proteins using mass spectrometry has expanded exponentially, from 1-10 proteins at a time, to 200-300, and now to up to 7,000 at a time. Our research discoveries have led to a drug development program with potential to treat epilepsy and other neurological disorders, as well as cancer and some infectious diseases. This program has produced many exciting lead compounds, and we are in the crucial but time-consuming process of identifying pre-clinical drug candidates to treat a range of diseases. This phase may take many years due to the need to improve drug delivery, safety, and specificity before a compound can be tested in human trials. Crucially, we are on the path to revolutionise the treatment of conditions like epilepsy, where there is no cure and 1 in 3 patients are not helped by current medications.

2015 Research Achievements:

→ Other scientists have often claimed that a future dynamin therapy for humans would be risky. However, we recently demonstrated that dynamin therapy for epilepsy and cancer is intrinsically safe for long term use. We showed that certain existing drugs, used for mood disorders for extended periods of time in patients over the last 30 years, also work by inhibiting the protein, dynamin in the brain. This is a second and new mode of action to their known role in dopamine receptors. It means that the more effective versions of dynamin inhibitors currently being developed by CMRI and the University of Newcastle should be safe in humans, once the chemistry and formulation of these new compounds has been perfected.

→ We have demonstrated that dynamin inhibitors can also treat simian haemorrhagic fever—which means these compounds may ultimately prove useful for human infection with Ebola and other viruses.

→ We published a series of high impact Methods papers aimed at teaching other researchers how to make and use dynamin inhibitors. These inhibitor compounds are now widely recognised in the broader scientific community for their research value and clinical potential.

→ Our epilepsy drug development program has established 3 new classes of dynamin and clathrin inhibitors, providing us with new lead compounds for further development.

WHAT’S NEXT: develop our epilepsy drugs to the point they can be used in clinical trials.

Infectious disease. This program has produced many exciting lead compounds, and we are in the crucial but time-consuming process of identifying pre-clinical drug candidates to treat a range of diseases. This phase may take many years due to the need to improve drug delivery, safety, and specificity before a compound can be tested in human trials. Crucially, we are on the path to revolutionise the treatment of conditions like epilepsy, where there is no cure and 1 in 3 patients are not helped by current medications.

2015 Research Achievements:

→ We were heavily involved in the design of the Proteomics facility in CMRI's new building and have helped run it efficiently as a 24/7 operation.

→ Developed expertise to further our studies of clathrin assembly, which is important for neurotransmission.

→ We identified a new subdomain of the protein AP180, which functions in endocytosis, a key process in neurotransmission.

→ Our work mapping signalling pathways for synaptic plasticity is ongoing, with new data continually leading us in new directions.

→ We've begun studying the protein, synuclein, which is involved in synaptic plasticity and is well known to have a role in Parkinson's disease.

→ Due to a wealth of findings, we've begun many collaborative projects on pre-synaptic plasticity and pathways that intersect with disease to explore these results further.

→ By the end of 2016, we should have a resource everyone can use to study their favourite protein in the brain.

WHAT’S NEXT: use our new understanding of nerve signalling to find leads for potential treatment of autism, Parkinson's and other diseases.

In the Synapse Proteomics Group, we are focused on answering fundamental questions such as how does the brain work? At the same time, we ask how a disease state, like epilepsy, can upset brain function.

This fundamental knowledge is then applied to identify new potential drug targets. The genes we study code for proteins involved in either neurotransmitter release (how chemical signals are sent from one brain cell to another), the shape of the synapse (the part of the brain cell that connects to another cell), or the ability of the synapse to adapt. Developing treatments for diseases requires knowledge of the genes involved, the proteins they code for, and how to target those proteins with drugs to change the disease state. A better understanding of neurotransmission, for example, will help us determine what goes wrong in a range of diseases like epilepsy, autism and Alzheimer's disease. It also tells us about normal learning and memory. We are also mapping the signalling networks between proteins inside the nerve cell and aim to add significantly to collaborative projects on pre-synaptic plasticity and pathways that intersect with disease to explore these results further.

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WHAT’S NEXT: use our new understanding of nerve signalling to find leads for potential treatment of autism, Parkinson's and other diseases.
Embryology

A gene regulatory network depicting interactions between genes involved in the development of the head.

Embryology Unit

Unit Head: Professor Patrick Tam BSc(Hons) MPhil PhD CBiol EurProBiol FAA FAHMS FRSB FRS
Deputy Director CMRI; NHMRC Senior Principal Research Fellow; Professor, School of Medical Sciences, Sydney Medical School, University of Sydney

Diseases Impacted by Our Research:

→ Birth defects in early development, especially the gut and associated organs
→ Head and face abnormalities, including Saethre-Chotzen syndrome, facial dysmorphology, and cleft lip and palate
→ Genetic diseases of the liver

The Embryology Unit studies how development occurs in order to understand what goes wrong in birth defects.

Current research focuses on the cellular and molecular mechanisms of body patterning during mouse development, in the context of the activity of the cascade of transcription control genes and signalling factors that have a key function in the formation of the head and face, as well as in the development of the gut and associated organs. We take a systems biology approach in elucidating the functional output of the gene regulatory work and signalling on embryo development, through the analysis of the combinatorial action of controlling genes (the interactome), the gene expression profile (the transcriptome) and the translational outcome (the proteome) of specific cell populations and single cells in the developing embryo.

We also explore the attribute of the processing of the messenger RNAs (the transcripts) by RNA binding protein complexes in gut development. In addition, we are gleaning new knowledge of cell differentiation, using a new type of stem cell we derived directly from advanced stage mouse embryos. We have optimised the method to direct the differentiation of these cells into gut cells that then specifically become liver and pancreas cells. The goal of this research is to develop a combination of cell-based and gene therapies for treating inborn errors of metabolism. This work is a collaboration with the Gene Therapy Unit in a joint effort of CMRI and The Children’s Hospital at Westmead of the Sydney Children’s Hospital Network.

Continued on page 32 ...
2015 Research Achievements:

→ We are gaining an understanding of the process of cells transitioning between dispersed and tightly packed states, which is important for organ development. Such changes in cell state also occur during cancer metastasises, when cells from a solid tumour are disseminated and then form a solid tumour again in another part of the body.

→ We have identified several key genes that are important for head and neck formation in the mouse and are working to understand the extensive gene regulatory networks they are a part of. We are all examining more closely the genes these key genes control, analogous to the cornerstones and the brick and mortar of a building respectively, to find out if when disrupted they may cause birth defects. Understanding these genes will enable us to alert clinicians of genes that may be relevant to human genetic diseases and which can be screened for errors in the specific gene in the clinic.

→ We are interested in mouse embryo development when the basic body plan is being established. At this stage, the embryo grows from about 600 cells in size to over 15,000 cells, and we learn from testing how these cells differentiate that there is a progressive increase in the complexity and diversification of developmental cell fates. We recently took a major step forward to examine a smaller population of these cells and have analysed in exquisite detail what parts of the genetic code are used by small groups of cells in the early embryo to drive how far they can differentiate. The results of this collaborative work, undertaken with the Cell Biology and Bioinformatics teams at the Shanghai Institute of Biological Sciences of the Chinese Academy of Sciences, are made available to the international community of scientists in this research area, whose future work can now build on our findings. Our next goal, which we plan to complete within the next two years, is to further increase the precision of these analyses down to the level of individual cells. Potentially, we can translate this knowledge to drive cell differentiation to generate clinically useful cells for implementing tissue therapies, modelling diseases, and testing the efficacy of drugs.

→ A significant advance was achieved in the study of the function of the RNA binding protein, RBM47. We have identified this as a key factor that binds RNAs in gut tissues. We have applied an innovative protocol to identify the RNA species targeted by RBM47 and the functional consequences of this molecular interaction. We found that binding mediates RNA editing that could produce an alternative form of the gene transcript, so two different proteins can be made from the same gene. The shorter protein is actually the working version.

→ Functional Genomics is critical for understanding what a group of functionally connected genes does, and we are building the capacity to do the necessary work following the discovery of disease-causing genes. We have already developed efficient genome editing capacity. Our research capability has been significantly boosted by the support of The Vector and Genome Engineering Facility and will be further enhanced by developing the infrastructure for the production of induced pluripotent stem cells, which are part of CMRI’s plan to establish a research cluster on pluripotent stem cells, which are part of CMRI's plan to establish a research cluster on the future of tissue engineering.

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Future Plans:

→ We’ve created a novel AAV that can directly deliver genetic material to neurons in the brain and are currently perfecting their function.

→ Finally, we’re looking into transduction and homologous recombination uses for AAV in the haematopoietic system.

→ Our first priority is to develop a library of AAV tools that have functional use in the clinic.

→ A secondary aim is to understand why these tools work, the biology of AAV. This has been a difficult field, yielding few results over the last half century, thus we maintain a functional focus for our studies.

Translational Vectorology (TVG) is the newest group to be formed at CMRI and was established at the end of 2015. The aim of the TVG is to develop the tools and expertise needed to speed up research and to help bring new gene therapy treatments for human diseases to the clinic as soon as possible.

The group focuses on developing new gene therapy vectors based on Adeno-Associated Virus (AAV) as tools for genome-editing and gene delivery. TVG is interested in developing these tools to target a broad array of tissue types and thus address a range of diseases, starting with those listed below but eventually moving into cystic fibrosis and other genetic diseases.

WHAT’S NEXT: develop our knowledge of cell differentiation for advancing cellular and gene therapy, disease modelling and testing for personalised therapeutics.
Many of the genes that cause eye disease are not known. We aim to discover the underlying disease genes in order to develop new treatment strategies, in many cases where no current treatment exists.

We use next-generation sequencing techniques and genomic investigations to pinpoint the disease genes. The functions of the genes and of the proteins they encode are then determined using cell-based and animal studies. Only when we understand how a gene and its protein work can we hope to find a cure. Disorders studied include: retinal diseases that affect the photoreceptor cells at the back of the eye; cataracts where there is clouding of the lens; glaucoma which can be associated with raised pressure in the eye; and conditions where there can be small or malformed eyes. Other genetic conditions are also studied where the causative disease genes are not yet known.

2015 Research Achievements:

→ We are developing a potential cell-based gene approach for investigating and treating retinal diseases.

→ There are currently over 60 genes known to cause developmental eye diseases. We established a genomic sequencing strategy for detection of these, resulting in a significant improvement in disease gene identification for patients with these conditions. This is now translated to clinical practice.

→ There are over 120 genes known to cause genetic retinal diseases including retinitis pigmentosa, Leber congenital amaurosis, and cone dystrophies. We successfully used a genomic sequencing strategy for detection of disease genes in these disorders. This is now under translation to clinical practice.

→ Use of genomics has markedly improved clinical diagnosis in many of these genetic eye conditions, and this is especially so where the eye problem may be part of a larger syndrome; this gives families early warning of additional health problems that will need to be addressed.

→ We are still finding many new genes that cause eye diseases such as cataracts, glaucoma and retinal diseases.

→ We are using cell-based studies to understand the function of these genes and the proteins they encode.

→ We’ve begun studying some eye diseases that are polygenic (many genes involved) with complex environmental factors, and are teasing out the roles of the individual factors. We need to make sense of the complexity in these diseases in order to better target therapies to particular genetic profiles.

WHAT'S NEXT: Develop gene or pharmacological-based treatments for retinal and other eye diseases

Diseases Impacted by Our Research:

Genetic eye disorders, including...

→ retinal disease such as retinitis pigmentosa

→ childhood cataracts

→ glaucoma

→ rare syndromes with a visual component

The Gene Therapy Research Unit is focused on the development of novel gene-based therapies for the treatment of genetic diseases in children. The Unit is a joint initiative of Children’s Medical Research Institute (CMRI) and The Children’s Hospital at Westmead.

Our primary goal is to realise the therapeutic potential of the current explosion of genetic knowledge. This not only requires a detailed knowledge of the many genetic diseases potentially treatable using gene therapy, but also the development of safe and efficient gene addition and genome editing technologies.

We have a special interest in diseases of the liver and bone marrow, as overcoming the challenge of repairing genetic errors in these tissues has exciting implications for treating a large number of conditions in infants and children. As described in last year’s report, we remain actively involved in working towards the initiation of clinical trials for SCID-X1 (an immune deficiency disorder) and ornithine transcarbamylase (OTC) deficiency (a urea cycle defect), which target the bone marrow and liver, respectively. In SCID-X1, also known as ‘boy in the bubble disease’, the aim is to use lentiviral vector technology to restore the ability of bone marrow cells to produce cells involved in immune system function, while in the OTC trial the aim is to restore the ability of the liver to convert highly toxic ammonia into urea. Both these trials involve academic collaborations with colleagues at the Institute of Child Health and University College, London, and are also drawing interest from biotechnology companies in the UK and US.

We are also involved in an ongoing gene therapy trial for children with brain tumours that are resistant to conventional therapy; this is a collaboration with the Children’s Cancer Research Unit at The Children’s Hospital at Westmead. The aim of this trial is to improve the resilience of bone marrow in children with brain tumours who are undergoing chemotherapy. This has the potential to allow them to withstand higher doses of conventional chemotherapy.

To underpin this clinical trial activity, we run an extensive pre-clinical laboratory research program. This program has two major components: the development of safer and more efficient gene transfer and genome editing technologies, and the testing of these in experimental models of human disease.

Continued on page 37 ...
2015 Research Achievements:

→ Professor Alexander was elected a fellow of the Australian Academy of Health and Medical Sciences in recognition of his contribution to biomedical research in the field of gene therapy.

→ Professor Alexander was appointed to the Scientific Advisory Committee of Dimension Therapeutics, a US company dedicated to the development of gene therapy for genetic liver disease.

→ In collaboration with Professor Tam, members of the Gene Therapy Research Unit have played a pivotal role in successfully establishing the Vector and Genome Engineering Facility and recruited Dr Leszek Lisowski from the Salk Institute to lead this exciting new initiative. Dr Lisowski is also establishing a new research group that will further strengthen gene therapy research efforts within CMRI and across the Sydney Children’s Hospitals Network.

→ In collaboration with colleagues at the Institute of Child Health and University College London, we have been awarded a large UK Medical Research Council grant to undertake pre-clinical toxicology studies designed to underpin a future gene therapy trial for infants and children with ornithine transcarbamylase deficiency, a urea cycle defect.

→ In addition to our established emphasis on clinical translation, we have increased our focus on commercial linkages and the generation of intellectual property (these will be detailed in the next annual report).

WHAT’S NEXT: Strengthen our interactions with the commercial sector to help speed the pace with which we can develop new therapies and move them through to clinical application.
Growing up in a small, country village in Hertfordshire, north of London, Associate Professor Hilda Pickett has always had a fascination with genetics and understanding DNA. After school, she turned that passion into a career, undertaking a degree in Biological Sciences (Genetics) at the University of Birmingham, before doing her PhD at the University of Leicester.

“It’s incredibly addictive. I’m constantly learning things; it’s constantly challenging; you have to be on top of the literature and you have to look at the bigger picture, but it’s really interesting,” Hilda says.

After a three year stint working at the University of Leeds in cancer research, Hilda moved to Australia in 2005, having accepted a role with Children’s Medical Research Institute (CMRI) as a Post-Doc in Professor Roger Reddel’s lab. In 2012, Hilda was running her own lab, the Telomere Length Regulation Group. The ultimate goal of her work is understanding the Alternative Lengthening of Telomeres (ALT) pathway of telomere maintenance and how it becomes activated in cancer cells. Right now, she is working on telomere sequence dynamics, how telomere variant repeats contribute to structural aberrations at ALT telomeres, and the molecular mechanisms responsible for telomere-telomere associations and recombination-directed replication.

“I want to understand in great detail various aspects of telomere molecular biology, with the aim to use these to develop cancer therapies. We’ve identified a number of mutations that predispose people to cancer, and we’re trying to understand how that happens,” Hilda said.

Hilda says the downside of research is the difficulty in obtaining funding, which leads to low job security. “I spend a lot of time writing grants so that I can continue to fund my lab.”

But Hilda says the rewards in return make it worth it. “You can get a bit jaded when things don’t work, but when they do, it’s just awesome,” she says. “It doesn’t matter the scale of the success, when you find something, it’s exciting and addictive.”

When Hilda isn’t in the lab, you can find her doing something outdoors. But what takes up most of her time is her home life. Seven weeks after giving birth to her, now 8-month-old daughter, Aurora, she was back in the lab. “Juggling work and home life can be difficult; research is definitely not a nine-to-five job. I’m lucky I have a supportive family!”

Hilda wants to spend the next several years publishing influential studies, eventually become more internationally recognised for her work, and become more involved in national research programs.

“I want to do really high quality research, using cutting-edge techniques and technology, to answer questions that are important and answer them well.”
In addition to accelerating research efforts within CMRI and the Westmead Hub with facilities such as the Bioinformatics Unit, CMRI provides important resources for scientists throughout Australia.

It operates CellBank Australia™, the only national repository of cell cultures, necessary for many fields of medical science. In addition, CMRI houses a major Biomedical Proteomics facility and three Australian firsts which constitute the ACRF Cancer Centre. These three facilities are: ProCan (the ACRF Centre for the Proteome of Human Cancer, which will open in 2016); the ACRF Centre for Kinomics; and the ACRF Telomere Analysis Centre, which officially opened in 2015.
ACRF Telomere Analysis Centre (ATAC)

The primary scientific focus of the ACRF Telomere Analysis Centre (ATAC) is concentrated on the study of telomeres, the structures at chromosome ends, and their roles in cell proliferation, cancer and ageing, with a secondary focus being to support a broad range of medical and biological research projects.

ATAC is the brainchild of a unique group of telomere researchers from a broad range of scientific and medical backgrounds and skill sets, including clinical haematology, medical oncology and laboratory-based research. This large consortium of telomere researchers utilises cutting-edge laboratory-based research. This large consortium of telomere researchers with a broad range of medical and biological research projects.

ATAC focuses on four key components of telomere-related research, including:

1. Telomere Length Analysis. ATAC will support collaborative epidemiological and clinical studies throughout Australia, in which telomere length is used as a biomarker.

2. Automated Microscopy. CMRI has pioneered the use of automated scanning for metaphase cells in telomere research, and the ATAC equipment will allow new faster image analysis procedures to be developed for analysing cells at all phases of the cell cycle.

3. High-Resolution Fluorescence Microscopy. The length of individual telomeres, telomere structure, and telomere-interacting proteins are all critically important for telomere function and research. The high-resolution microscope technology at ATAC greatly enhances the researchers’ ability to study these characteristics.

4. Live Cell Imaging. Telomere structure and function changes dynamically during the cell cycle. Technology at ATAC will put our research groups at the forefront of this field by providing researchers with the ability to study telomere dynamics in live cells.

2015 saw the full establishment of ATAC with the installation of the Centre’s equipment, which was supported by the Australian Cancer Research Foundation (ACRF) and the Ian Potter Foundation. CMRI researchers could then take full advantage of the custom-built laboratory space ATAC occupies on Level 2 of CMRI’s Stage 1 expansion. On May 21, ATAC was officially opened by The Hon. Pru Goward, NSW Minister for Medical Research.

Within six months of its official opening, ATAC’s impact on research was demonstrated in the first published research paper in which ATAC microscopes were used. The paper, published in the journal Cell Reports by members of CMRI’s Cell Biology Unit and their collaborators, describes new findings on key regulators of the protein responsible for telomere maintenance in the majority of human cancers. The results presented include data from a new automated imaging approach developed at ATAC this year.

Bioinformatics is the application of information technology to medical and biological research.

The genetic makeup of an individual, the genome, can be represented as a long string of four different letters. If these letters were to be printed out, the genetic makeup of one person would fill an entire bookshelf. At CMRI, our research into cancer, embryology, cell signalling, and gene therapy often requires collecting and comparing many hundreds or thousands of genomes, in order to find the places where changes in the genetic code lead to disease. Through CMRI initiatives, such as the ACRF International Centre for the Proteome of Human Cancer (ProCan), we explore the effects of those genetic changes on the proteins our body produces in order to understand how the genetic change leads to the disease and thus how we can treat it.

Both genomics (identifying the complete genetic makeup of a person) and proteomics (identifying the proteins produced by the genome and how they work in the body) generate vast volumes of data. Sophisticated computational techniques are needed in order to acquire, store, manage, visualise, analyse, and interpret. This integral component of many of our research programs is undertaken by the CMRI Bioinformatics Unit.

The CMRI Bioinformatics Unit, under the leadership of Associate Professor Jonathan Arthur, works collaboratively with CMRI Research Units and Groups on projects involving large, complex data sets, including:

→ comparing the genetic makeup of cancer tissue with healthy tissue to identify the genetic changes that lead to cancer;

→ examining which parts of our genetic makeup are switched on and off at different times during development and how changes in that pattern of expression may lead to birth defects;

→ developing software to automatically process thousands of high-resolution microscope images in order to accurately quantify the properties of cancer cells;

→ identifying proteins used by the brain and central nervous system to send and receive messages throughout the body, and exploring how their dysfunction leads to diseases such as epilepsy;

→ understanding where and how gene therapy alters the genetic makeup of a cell to correct disease-related genetic changes.

The CMRI Bioinformatics Unit actively contributes to the development of bioinformatics capability across the Westmead Hub and works collaboratively with other bioinformatics initiatives throughout NSW and Australia.
Human or animal cells grown in culture (cell lines) are an integral part of health and medical research. They serve as a model system for the study of cancer and many other diseases and are used in the discovery of new treatments. Without proper handling, cell lines can become contaminated, which can negatively impact any research conducted using those cell lines. For this reason it is critical for Australian researchers to have easy access to high quality, validated cell lines for their research.

CellBank is Australia’s only national cell line repository, providing Australian scientists with ready access to validated cell lines and associated quality control services. CellBank Australia collects novel cell lines, developed by Australian researchers, submits these cell lines to rigorous testing to confirm their integrity, and then distributes the cell lines to researchers throughout the world.

CellBank Australia also distributes, throughout Australia and New Zealand, more than 700 of the most commonly requested cell lines from the European Collection of Authenticated Cell Cultures (ECACC) at Public Health England, a major international cell line repository based in the UK. This ensures that a wide range of authenticated cell lines are readily available for use by Australian scientists.

In addition, CellBank Australia offers a variety of cell line-related services including STR profiling, Mycoplasma testing, Culture and Return, and Secure Storage. It is also part of CellBank’s goals to create awareness of the issues surrounding cell line integrity and contamination and to assist with the education of the Australian scientific community about these matters.

CellBank Australia has International Depository Authority status, under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This means CellBank Australia is the only site in Australia that can provide secure storage for human and animal cell lines and hybridomas that are the subjects of patent applications.

CellBank Australia receives funding from the Cancer Institute NSW and was also the recipient of a National Health and Medical Research Council Enabling Grant from 2005 to 2010. It was established in 2005 with support from Cure Cancer Australia Foundation and a major donation by Lady Mary Fairfax via the National Breast Cancer Foundation.

Visit cellbankaustralia.com.au
Only 18 months separated Sophie from her older brother, Hamish. Both were diagnosed with brain cancer, Hamish in 2009 and Sophie in 2011. Hamish died when he was 15 years old.

"He's a constant reminder, he's always there, egging me on," Sophie says.

Sophie underwent a gruelling regimen of radiation and chemotherapy before she went into remission. Now aged 18, she's working and attending university. "I’m studying nursing and really enjoying it." She seems to have found her calling, which is caring for others.

CMRI’s Director, Roger Reddel, was affected by their ordeal. He said, "During a memorial service like Hamish’s, there are lots of things that you can’t help thinking about, such as the importance of family and of communities rallying to support people in difficult circumstances. And nothing else could more strongly reinforce the significance of what each and every one of us does here at CMRI, and why we come to work each day."
Biomedical Proteomics

Biomedical Proteomics at CMRI is a collaborative research platform providing high-throughput approaches to study the proteins in our cells and tissues. Understanding the structure and function of each protein in the human body and the complexities of their interactions is critical for the development of effective diagnostic and disease management tools in the future. The Facility supports scientists at CMRI and the Westmead Research Hub by offering not only access to sophisticated equipment and methodology but also expert advice in assessing the feasibility of new research projects and programs and developing strategies to implement them.

CMRI took an early lead in proteomics in 1998, and has been retaining and nurturing talent in this area for the past 16 years. With the completion of Stage 1 of CMRI's building redevelopment in mid-2015, Biomedical Proteomics and the ACRF Centre for Kinomics were relocated to a large, modern, area for the past 16 years. With the completion of Biomedical Proteomics at CMRI is a collaborative research platform providing high-throughput approaches to study the proteins in our cells and tissues. Understanding the structure and function of each protein in the human body and the complexities of their interactions is critical for the development of effective diagnostic and disease management tools in the future. The Facility supports scientists at CMRI and the Westmead Research Hub by offering not only access to sophisticated equipment and methodology but also expert advice in assessing the feasibility of new research projects and programs and developing strategies to implement them.

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Biomedical Proteomics currently houses a total of seven advanced liquid chromatography-mass spectrometry (LC-MS) systems. Four were purchased with generous funding from the Australian Cancer Research Foundation (ACRF) and the Ramaciotti Foundations to equip the new ACRF Centre for Kinomics (ACRF-CFK). Major funding by the Cancer Institute NSW, the Australian Research Council Linkage Infrastructure, Equipment and Facilities scheme, and the Ian Potter Foundation provided two additional LC-MS systems.

This massive investment in new technologies has enabled the rapid progress of large-scale, long-term studies with publication of several papers in 2015. In addition, in partnership with SCIEX, several research and development projects were initiated that have opened up opportunities for scaling up joint research efforts. The Facility has also established an ongoing series of seminars, workshops and other educational and training opportunities for staff and students.

'The Research Hotel' was introduced with the Stage 1 redevelopment. This means we have capacity for up to 20 visiting researchers to stay and complete their proteomics studies at CMRI. This includes access to the wet lab, instrument space, data lab and conference room, all while receiving expert research and technical advice from CMRI staff.

Our goals are to maximize use of existing capacity, maintain the highest standards and international reputation, while enabling researchers from anywhere in Australia to benefit from our facilities.

In 2015, Biomedical Proteomics hosted the second international Chemical Proteomics symposium (cmri.org.au/cps), which covered a broad range of topics related to modern Medicinal Chemistry and Proteomics, with the intention to engage researchers from multiple disciplines and promote networking and collaborations. Key international and national speakers presented, such as Dr Ludovic Gillet from ETH Zurich, to a crowd of over 100 scientists. The goal is to continue to grow this event and host it biennially in Sydney.

The ACRF Centre for Kinomics™

The ACRF Centre for Kinomics (supported by the Ramaciotti Foundations) officially opened on 23 September 2012.

The ACRF-CFK – a joint venture of CMRI (Biomedical Proteomics) and the University of Newcastle (UoN) (Medicinal Chemistry) — is an Australian-first that provides an entirely new chemical biology approach to the understanding of cancer therapeutic drugs and ways to improve them.

This significant, non-commercial initiative builds upon demonstrated research excellence, leadership and successful collaborations between scientists from CMRI and UoN. The ACRF-CFK is equipped with state-of-the-art instrumentation, thanks to generous funding from the Australian Cancer Research Foundation (ACRF) and the Ramaciotti Foundations.

The Centre’s main focus at present is to facilitate a smooth transition to a fully functional, large scale national research platform, providing technologies and support for the discovery process that underpins progress in many of CMRI's research areas. The priority is to ensure that these facilities realise their full potential to enhance Australian medical science and drug design and discovery.

Through the development of Kinomics technology and through its collaborations with research teams across Australia, the Centre will enable a better understanding of current therapies and their unwanted side effects. More importantly, the Centre will aid the development of new drugs for a broad spectrum of human diseases, many of which are currently without any effective treatment.

The Australian Cancer Research Foundation (ACRF) Centre for Kinomics (supported by the Ramaciotti Foundations) officially opened on 23 September 2012.

The ACRF-CFK – a joint venture of CMRI (Biomedical Proteomics) and the University of Newcastle (UoN) (Medicinal Chemistry) — is an Australian-first that provides an entirely new chemical biology approach to the understanding of cancer therapeutic drugs and ways to improve them.

This significant, non-commercial initiative builds upon demonstrated research excellence, leadership and successful collaborations between scientists from CMRI and UoN. The ACRF-CFK is equipped with state-of-the-art instrumentation, thanks to generous funding from the Australian Cancer Research Foundation (ACRF) and the Ramaciotti Foundations.

The Centre’s main focus at present is to facilitate a smooth transition to a fully functional, large scale national research platform, providing technologies and support for the discovery process that underpins progress in many of CMRI’s research areas. The priority is to ensure that these facilities realise their full potential to enhance Australian medical science and drug design and discovery.

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WHAT ProCan™ CAN DO

Freddy was born with cancer. His mother noticed something wrong in hospital, but it took 6 months of travelling around Australia from their home in Alice Springs to Adelaide and then to Sydney to get the diagnosis—a rare cancer that was difficult to treat.

Freddy endured over a year of gruelling chemotherapy. He never knew what it was to be a normal toddler. Worse was the fear and uncertainty his family faced; not even his four-year-old brother thought he would live. Until, finally, the tumour went into remission. Freddy's story has a happy ending, but too many don't.

Cancer is an experience no family wants to endure, yet over 600 children are diagnosed with cancer in Australia every year.

Imagine a report that could give your doctor all the information they needed to choose the best treatment option for your child— which drugs would be effective and which wouldn't, as well as which clinical approach would give them the best possible chance of survival. This is the vision of ProCan.

ProCan will eliminate the guesswork and potentially bypass dozens of pathology tests. Within 24 hours, a biopsy sample the size of a grain of rice can be analysed, scanning for tell-tale proteins inside the tumour, which are then compared, using sophisticated algorithms, to a library of over 70,000 cancers from all over the world.

This library will be created in an ambitious, seven-year project led by Children's Medical Research Institute using the most advanced technology available. When complete, ProCan will enable the following answers: a detailed molecular diagnosis for each patient and recommendations for treatment based on what has worked for previous cancers with the same molecular markers.

This will give doctors a powerful resource to provide children and their families with an evidence-based, personalised treatment plan within days.

Fast, accurate diagnosis. Increased chance of a cure. Through ProCan we can help more children and their families overcome cancer.

How?

ProCan (the ACRF Proteome of Human Cancer facility) is a world-first. New technology called PCT-SWATH mass spectrometry will be used to rapidly and simultaneously measure the precise levels of many thousands of proteins in very small cancer biopsies.

Advanced computer analysis techniques will then be used to compare the protein data with the information that is already available for each cancer, including clinical records, pathology test results, genetic analyses and any previous responses to cancer treatment. Based on the huge library of information this will create it will then be possible, for any new cancer patient, to make a precise analysis of cancer type and its molecular subtype, and to identify which of the currently available cancer treatments are most likely to be successful.

The Centre will be led by CMRI Professors Phil Robinson and Roger Reddel in partnership with technology experts, such as Professor Ruedi Aebersold in Zurich, and working in partnership with leading cancer researchers throughout Australia and around the world.

Diagnosis, discoveries, new treatments …

In addition to this game-changing approach to cancer diagnosis and treatment planning, ProCan has the potential to discover new cancer treatments.

The public library of information created at the Centre will foster collaboration and fast track cancer research by increasing our overall understanding of every cancer type. It will also boost our ability to develop new, more effective, and precisely targeted cancer treatments by revealing the changes that occur in different cancers.

What's more, the potential of this technology doesn't stop at cancer. We can apply the same approach in future for other diseases. The possibilities are far reaching.
CMRI was established from grass roots community support in 1958 and still relies heavily on the support of individuals and community groups to achieve its long term research goals.

Two-thirds of the Institute’s revenue comes from private fundraising sources, including the Jeans for Genes® and Great Cycle Challenge campaigns, community fundraising, bequests, direct marketing and a long-established investment fund.

The following pages highlight the achievements of CMRI’s fundraising programs in 2015 and acknowledge supporters who gave generously of their time and money to help create a healthier, brighter future for all children.
Jeans for Genes®

Jeans for Genes is one of Australia’s most recognised and loved charity campaigns and is a major fundraiser for Children’s Medical Research Institute.

2015 saw a continued upward trend for the campaign, with it generating the highest net returns of the past three years. Australians everywhere got behind the day by selling merchandise and holding events in their offices, clubs and social groups, while over 2,300 schools took part, involving more than 1.5 million children.

The day itself was celebrated across the country in 60 locations, each brought to life thanks to more than 1,000 volunteers, including staff from CMRI and members of our beloved committees. Merchandise sales and donations from the public at these events heightened the publics’ awareness of Jeans for Genes and made the day an occasion that attracted overwhelming print, television and radio support.

Our long-standing retail partners once again played a significant part in gathering donations and increasing the awareness of Jeans for Genes. Special thanks goes to Sydney Trains and also to Big W, Outback Steakhouse, HCF, Lowes, Auswide, Newcastle Permanent and Jeanswest, all of whom contributed significant instore and financial support to our campaign. Staples once again provided generous assistance to our schools program, which is very important to us, and Star Alliance offered travel incentives which were used to great effect in encouraging our supporters to register to fundraise.

Australia’s media outlets also continued to provide generous support, donating more than $2 million in pro-bono media space and air-time, which enabled us to promote the event and, importantly, keep the brand in the public’s mind.

Our 2015 campaign ambassador, Jodi Anasta, generously donated her time to appear in media interviews leading up to the big day and on Jeans for Genes Day itself, where she worked tirelessly to promote us. Jodi also attended the jeans for Genes Gala Dinner and spoke genuinely about her affection for us.

As part of a re-design of the jeans for Genes website, we introduced an exciting innovation called peer-to-peer fundraising. This enabled supporters to engage their friends and family online, providing a new way to raise vital funds. In its first year, this innovation was well received by new and old supporters, which gives us great confidence that online fundraising will prove successful for the cause.

In 2016, we’re looking to build on all of the groundwork from 2015, especially our new websites’ functionality and the peer-to-peer fundraising channel, along with a continuation of the popular advertising creative. Additionally, we have some exciting innovations to introduce to the campaign, especially in schools.

Friday 7th August 2015

PLEASE DONATE at jeansforgenes.org.au
Gala Dinner - Welcome to Las Vegas!

On Saturday 22 August 2015, bright lights, glitz and glamour were brought to Sydney, Las Vegas Style! Raising over $200k, the annual Jeans for Genes Gala Dinner supports our research into birth defects, cancers and genetic diseases.

It was a highly memorable evening with stunning entertainment and great food. Wendy Harmer, our Mistress of Ceremonies, injected her unique humour into the event, keeping the night full of energy. We were also pleased to welcome back Ray Hadley OAM as our Auctioneer. Ray did a brilliant job at inciting competitive bidding in support of paediatric research.

We were once again amazed by the generous support of renowned Australian artists, sponsors and special guests. We are especially grateful to Rachel, Levi and Clay Bockman for sharing with us their personal journey with brain cancer. What a brave family. After all they have been through, we were moved by their wonderful positivity and commitment to raising funds for research which will help other families in the future.

Professor Ian Alexander, who heads our Gene Therapy Research Unit, spoke about the major advances in research technologies and their impact on developing new treatments for previously incurable genetic diseases.

True to the Vegas theme, the entertainment was bold and full of famous faces, with performances from the Village Performing Arts Group as well as some of Australia’s best talent, including Danni Da Ros as Celine Dion, Briden Starr as Beyoncé, and the talented Louie George. A transcending aerial artist had us soaring to new heights, and the Tom Jones Band had us dancing until the lights came on.

Thanks again to our major sponsors: Delta Airways, Burwood Press, Decorative Events, Woolworths Limited, Hilton Hotel, John Boston, Champagne Duperrey, Krondorf and Stonyfell.

A special thanks to our fabulous volunteer Gala Dinner Event Committee Members: Patsy Cadell, John Glover, Rod Glover and Patti Payne. They worked tirelessly behind the scenes to make the event such a great success.

Finally, none of this would have be possible without the kindness, compassion and ongoing commitment of our distinguished guests. Medical research is the only way that we can tackle the big questions around life-threatening diseases and find answers sooner. Our thanks to all involved on the night and for once again sharing our vision and bringing greater hope for the future for families and children.

On Sunday 22nd September 2015, hundreds of walkers pounded the pavement at Parramatta Park for the inaugural Ks for Kids event. Over $47,000 was raised.

Participants could choose from a 6 km or 30 km walk challenge and were cheered along by many upbeat and enthusiastic volunteers on the track. Spirits were high when walkers were presented with a Ks for Kids coloured slap band after each lap.

A beautiful sunny and warm spring day attracted even more visitors to our family-friendly event in the park. Kids were kept well entertained with activities such as jumping castles, animal farm, face painting and balloon twisting, while the adults enjoyed the live entertainment on stage and took advantage of the great food and coffee trucks available on site.

CMRI researchers were busy talking to the crowds at the CMRI talk tent and were the heroes of the day as they joined in with a few laps.

The day was a great success, so thank you to all who participated!

In 2016, we will be launching two new Ks for Kids in Canberra and the Central Coast, as well as holding our successful Western Sydney event again. For more information on Ks for Kids, visit the website ksforkidswalk.org.au.

More than 8,000 participants got on their bikes to fight kids’ cancer as part of the Great Cycle Challenge in 2015.

The event raised an incredible $2.6 million in 2015, bringing the total raised by this event to nearly $6 million over the last three years.

The event asks participants to set a personal ride goal and fundraising target and work towards it throughout the month.

Special thanks to our GCC Partners in 2015, including the firm Ridley, Jackson Teece and Lahey, and to Executive Channel.

The Great Cycle Challenge will be held again in October 2016. To find out more about Great Cycle Challenge and to get involved visit greatcyclechallenge.com.au.
Community Fundraising

CMRI relies on the devoted support of community groups and individuals, who host a wide range of fundraising activities and events, such as the annual Earle Page College Coast Run and Earle Page College Fashion Show. We are ever grateful for their energy and enthusiasm and the funds they raise.

Our amazing CMRI committees are the foundation of our community fundraising and public awareness efforts. They are a model for community involvement, and each year their tireless work benefits all of our medical research programs. Some highlights from 2015, were:

→ Vaucluse Committee Bill Waugh Memorial Cup Tennis Day
→ Canberra Committee’s Annual Luncheon
→ Hills Committee’s Mothers’ Luncheon
→ Strathfield Committee’s June Gala Dinner
→ Wagga Wagga Committee’s “Out in the Garden” country tour, Christmas Fair
→ High Tea – Mudgee, Gerringong, Strathfield Committees
→ Gerringong’s Famous Annual Quilt Show
→ Gosford Committee’s Christmas Garden Party
→ Port Hacking Luncheon and Fashion Show and Jazz for Genes
→ Taree Baby Show
→ Melbourne Cup luncheons, sweeps and raffles held by Kangaroo Valley, Racquet and Northern Beaches committees
→ Golf Days – hosted by Northern Beaches, Strathfield, Port Hacking Committees
→ Card Days – Racquet and Northern Beaches Committees

→ Quiz Nights – Strathfield and Gosford Committees
→ Discovery Day catering – Beecroft Committee
→ Maroota Fashion Shows
→ Judith Hyam Memorial Trust Fund – fashion shows, weekend in Gloucester, Christmas in July, Silver Anniversary Dinner

Other wonderful community supporters also include: Trivett Class BMW Parramatta, with 13 years of support for the Golf Day; Rotary Club of Cessnock Wine Country; and Treasury of Craft, with 23 years of dedicated fundraising via craft stalls.

Major Supporters & Partners

Children’s Medical Research Institute and Jeans for Genes are supported by a wide range of individuals, businesses, trusts and foundations. A full listing of key supporters is provided in the addendum to this report available on our website.

We especially thank our major supporters, including Mr James Fairfax, The Australian Cancer Research Foundation, YuHu Group, Memocorp, Ian Potter Foundation, Mrs Joan M Barnet, Woolworths Support Office Bella Vista, Franklins, J.J. Richard & Sons and In Memory of Tay Tee Peng.

We also acknowledge the long term support of the Judith Hyam Memorial Trust Fund for Cancer Research whose generosity has enabled the continuance of two named positions in our Cancer Research Unit. The work of other young PhD students and scientists at CMRI is supported by scholarships from a number of generous sources: Yass Memorial Scholarship, Douglas and Lola Douglas Scholarship, Denise Higgins Scholarship, Rosemary Raymer Scholarship, Sir Norman Gregg Fellowship, and the Star Alliance Travel Scholarship.

Our corporate partners are important to our fundraising efforts, and we are fortunate to have long standing relationships with a number of companies. Some of our corporate supporters provide a combination of pro bono services and financial sponsorship. Particular thanks goes to Burwood Press, Technology One, Addisons Lawyers, Allens<Linklaters, Star Alliance, Cherry Media, Vinva Asset Management, Standford Brown, Younis & Partners, and Sciex for their generous support throughout 2015.

In the year ahead, we will continue to develop new and existing partnerships, and look forward to even bigger achievements together in years to come.

Our Loyal Supporters are GameChangers

We thank and acknowledge the contribution of our loyal supporters who have pledged regular financial support for CMRI. Previously known as “Discovery Partners”, this group of people are farsighted and generous. In recognition of their ongoing commitment and vital role that they play as an essential part of our team, we will be referring to them from now on as “GameChangers”.

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Bequests - Leave the Gift of Love Behind

One of the most life-changing ways you can support CMRI is to leave a bequest in your will; it's a lasting legacy that will benefit future generations of children. Bequests are a vital source of income for CMRI, and we are always humbled by the generosity of our supporters who have left us a gift in their will. Your bequest will allow us to continue our world-leading research into childhood diseases to bring more effective treatments and cures to children everywhere.

Denva Barber has been a supporter and a volunteer at Children’s Medical Research Institute (CMRI) for over 15 years, and this is why she is leaving love behind.

“I first visited CMRI in February 1997 as part of a ‘Discovery Day’ tour. I thought it was a marvellous place. It was reassuring to see the spirit of communication among the scientists and their willingness to share research internationally. Everyone wants to find answers, treatments and cures.”

Denva, always a hard worker, spent 40 years in various roles for the Service and Electricity Commission and then Canterbury Hospital. After her tour of CMRI, she signed on as a volunteer, assisting with community relations, and says, “I will keep going until I can’t. I like keeping busy. I’ve since served on an ethics committee at CMRI, which was something I never expected to do. I enjoyed it very much and, from reading the scientists’ reports, learned more about the great work happening here.

“I was also impressed by the credible financial management of CMRI, how it is for the long term. I don’t have any children of my own, but CMRI’s research has the potential to help everyone, children and adults. That’s why I’ve decided to leave a residual to CMRI in my will.”

Denva will be leaving a loving gift behind, a gift that will benefit generations to come.

Apart from accidents, the leading cause of death in children under 4 is birth defects and genetic disease and for ages 4 to 14 it’s cancer.

Children’s Medical Research Institute is working hard to address these diseases. We focus on four main areas where we’ve achieved world-class excellence: cancer, neurobiology, birth defects, and gene therapy. We believe that no disease, whether it is cancer or a genetic disorder, is unstoppable. With your help, together we can beat childhood diseases.

If you would like to learn more about CMRI’s work or about leaving a gift in your will, please contact 1 800 436 437 or email bequests@cmri.org.au. You can also visit our website, cmri.org.au.

Sir Lorimer Dods, co-founder of CMRI, 1958
“At the ultrasound is where I got the news that my baby will possibly need an operation after birth,” said Ajax’s mum, Aimee. “They had detected a gap in his palate. If I am being completely honest, prior to this pregnancy I had never heard of cleft lip/palate.”

“It broke my heart, the idea of him having to have any kind of surgery after being born... I broke down and cried for a while because the realisation that he was going to have a genetic defect on his face was overwhelming. All I could think of is how I want to protect my baby... Will he be in pain? How will this impact the rest of his life?”

“Ajax was born with a cleft lip and palate and he is the most beautiful boy. The hard part was watching him go in for surgery and to have his face change after surgery. We had bonded with him while he had his cleft, so in a strange way it was a little sad to see it go. He is now two and just recently had his second operation.”

Isn’t he gorgeous?
Commercialisation

CMRI encourages its research staff to pursue opportunities for translating their discoveries into clinical and health applications, including generating commercial outcomes.

CMRI’s Intellectual Property Policy promotes the protection and development of Intellectual Property (IP) and shares commercial returns between the Institute, the Inventor and the relevant Laboratory or Facility.

IP surveys are conducted on average every two years, seeking to identify new IP, indicate strategic directions for translational research and to educate staff about IP and commercialisation issues. CMRI established its own new “fund” in 2015 to invest in commercialisation activities. An evaluation and investment framework is being developed that will further promote the pursuit of these opportunities amongst CMRI researchers and which will also look to leverage external funding opportunities that may be available.

Currently, CMRI generates commercial returns from the sale of proprietary research reagents and antibodies, distribution of unique cell lines and royalties from licensing patented technologies. Although returns are modest at present, growth of this income stream is a key strategy for CMRI. Several research programs are developing IP which is being patented and it is hoped that the opening of the Vector & Genome Engineering Facility, as well as ProCan, will generate many exciting new developments.

Some Key CMRI-Partner Relationships

**Kids Cancer Alliance**
- Children's Cancer Institute
- The Sydney Children’s Hospital Network
- University of New South Wales
- The University of Sydney

**Westmead Research Hub**
- The Westmead Institute for Medical Research
- Kids Research Institute
- The University of Sydney
- Institute of Clinical Pathology and Microbiological Research (ICPMR)
- Western Sydney Local Health District

**Sydney Health Partners**
- The University of Sydney and Affiliated Medical Research Institutes
- Western Sydney Local Health District
- Sydney Local Health District
- Northern Sydney Local Health District
In August 2014, the first stage of CMRI’s plans for redevelopment of its current building was completed. A seven-storey tower, funded by a $20 million capital grant from the New South Wales Government and from very generous, private donors, was opened by NSW Premier Mike Baird and Minister for Health Jillian Skinner.

Since then, CMRI has established several facilities in the new tower. The ACRF Australian Telomere Analysis Centre was opened in March of 2015; the Biomedical Proteomics Facility of CMRI (a Core Technology Facility of the Westmead Research Hub) was relocated into the tower in September of 2015; and a cutting-edge Vector and Genome Engineering Facility was launched in March of 2016.

CMRI will open a new facility, ProCan™, later this year. ProCan is an exciting new project to map the human cancer proteome, analysing the protein content of thousands of tumour samples with newly available technology. The opportunity to invest in ProCan and scale up its operations, as well as diversify into other areas of disease, means CMRI needs to progress its second stage of building redevelopment as soon as possible.

CMRI’s strategic plans call for complementary expansion of functional and translational genomics expertise and drug discovery capabilities. CMRI’s redevelopment is part of ongoing development plans for the whole Westmead Precinct, creating a world-leading centre for health and medical research. CMRI is exploring opportunities to share space and resources with other organisations on the campus, enabling access to cutting-edge equipment for researchers, engaging university students, and increasing the potential for inter-disciplinary collaboration.

CMRI has plans to redevelop its building over the next decade from its current two storeys to seven or more storeys in a total of five stages, with planning approvals already received. Once completed, the redevelopment will significantly grow our ability to make discoveries and speed up the search for cures and treatments for childhood diseases.

A major part of Stage 2 funding will be sought from government sources to cover building construction costs, with private philanthropy an essential component to fund the specialised facilities, equipment and fit-out of new spaces to support our strategic initiatives. This second stage will commence as soon as further funding is committed. Stage 2 will also leverage the full benefits of Stage 1, by taking advantage of certain services features and expanding the areas opened up in the first stage.

The CMRI Building Foundation was established to identify and approach individuals and organisations that might support CMRI’s expansion and strategic investment into these types of new initiatives, and the Foundation organised several events in 2015.

We would like to thank everyone who contributed to the completion of Stage 1: Mr Len Ainsworth for his generous donation of $5 million; YuHu Group for their $1 million donation; as well as MemoCorp. We thank 2GB for their assistance with fundraising for the building redevelopment. The radio station and two key hosts, Ray Hadley and Alan Jones, broadcast from CMRI in February, with surprise guest Minister for Health, Jillian Skinner, taking a turn at the microphone. Thanks also to the Canberra Committee of CMRI for their fundraising efforts on behalf of the Building Foundation. We would also like to thank CMRI Board Member and Building Foundation Member, Mr Bruce Fink, and his wife, Lauren, for hosting a very successful fundraising event at their home in October 2015. We thank the following people for their support at that event: In Memory of Tay Tee Peng, Monday Morning Cooking Club, Mr & Mrs Danny and Lisa Goldberg, Shand Foundation, Mr John Landerer, Barkam Investments P/L, Mr & Mrs Ian and Michelle Fischl, Mr & Mrs Phil and Vivien Green, Mr & Mrs Allan and Sharon Vidor, The Ivany Foundation. And special thanks to Diandra Edmondson, a young lady battling genetic disease who shared her story with guests and reminded everyone why CMRI’s work is so essential.

If you would like to contribute to our redevelopment, please visit cmri.org.au/redevelopment or contact Virginia Judge, Deputy Chair of the Building Foundation on (02) 8865 2921.
CMRI is an independent research institute based in Westmead, NSW.

The Institute employs approximately 160 people, including 120 full-time scientists and PhD students, as well as operational and administrative support staff and a team of fundraisers. CMRI is a public company, limited by guarantee, and a registered charity. The organisational structure of CMRI reflects its corporate governance and areas of responsibility.
The role and responsibility of the Board is to identify the critical aspects of organizational governance and to manage the overall business and affairs of CMRI.

Under the Constitution of CMRI, Board members are elected or appointed for three year terms and officer positions are voted on annually. More information on each board member is available online at cmri.org.au/Board and in the Addendum to the 2015 Annual Report.

Directors in Office (as of May 2016):

**Professor Frank Martin**

*MBBS FRANZCO FRACS AM Oph*, President

Professor Martin is currently President of the Asia-Pacific Society of Paediatric Ophthalmology and Strabismus and the International Strabismus Association. He serves on CMRI’s Audit and Risk Committee, Finance and Investment Committee, Intellectual Property Committee, is Chair of the Nominations and Remuneration Committee, and an Executive Member of the CMRI Building Foundation.

**Mrs Carolyn Forster**

*(OAM)*, Vice President

Mrs Forster worked in the Federal Parliament for 11 years, in the Senate, the House of Representatives, and the Ministry and is a former President of CMRI’s Canberra Committee. She is currently the Australian Delegate to the WFFM. She serves on CMRI’s Finance and Investment Committee, Audit and Risk Committee, and Nominations and Remunerations Committee, and is President of the CMRI Building Foundation.

**Mr Jeremy Waine**

Treasurer

Jeremy Waine is an investment banking and financial services professional with more than 15 years of experience with leading Australian and international companies, including UBS Investment Bank, CBA, Westpac and GE Capital. Jeremy joined the CMRI Board in 2016 and serves as the Treasurer. He is also Chairman of the Institute’s Finance & Investment Committee and a member of the Audit & Risk Committee.

**The Hon Craig Knowles**

*(OAM)*

Mr Knowles is the Chair of the Murray-Darling Basin Authority. He was a senior Minister in the New South Wales Government for 10 years, including serving as Minister for Health (1999–2003).

Continued on page 73...
Mrs Patricia Payne

Mrs Payne is currently foundation President of the Women for Pharmacy network and the Australian nominee to the Board of Directors of the Community Pharmacy Section of Federation Internationale Pharmaceutique. She helped form the Hills Committee of CMRI in 1991 and has been its President ever since. She serves as a member of the institutional Biosafety Committee.

Clinical Professor Graeme Stewart

Professor Stewart was appointed as founding head of Immunology at Westmead Hospital in 1980 and is the Inaugural Director of the Institute for Immunology and Allergy Research, one of the four founding research groups of the Westmead Millennium Institute. He serves as Chair of CMRI's Intellectual Property Committee.

Professor Roger Reddel

Professor Reddel is a Fellow of the Australian Academy of Science and in 2011 received the NSW Premier's Award for Outstanding Cancer Researcher of the Year. He heads CMRI's Cancer Research Unit and has been the CMRI Director and Lorimer Dods Professor, Sydney Medical School, University of Sydney since 2007. He serves on CMRI's Finance and Investment Committee.

Mr Albert Wong

Mr Wong is Chairman of Winmar Resources Limited and Deputy Chairman of Prima BioMed Limited and Kimberley Diamonds Limited. He has been a Member of the Australian Stock Exchange since 1988 and was the principal of Intersuisse Limited until 1995 when he established the Barton Capital group of companies, including eStar. He serves as an Executive Member of the CMRI Building Foundation.

Mr Bruce Fink

Mr Fink's career spans 25 years across various fields in the entertainment industry, including cinema and television production. In 2002, Mr Fink established and currently chairs the privately held Bickham Court Group of Companies and is also a co-founder of Media i. He serves on CMRI's Finance and Investment Committee, Audit and Risk Committee, and is an Executive Member of the CMRI Building Foundation.

Dr Luciano Dalla-Pozza

Dr Dalla-Pozza is Department Head and a Senior Staff Specialist of the Oncology Unit at The Children's Hospital at Westmead. He is an active member of numerous subspecialty societies focused on the care of children and adolescents with cancer.

Mr Michael Loughman

Mr Loughman is the Head of ANZ Private NSW & ACT, which is the Private Banking and Private Wealth Division within ANZ Bank. Mr Loughman is a Banking, Finance and Wealth Management professional with a career spanning 18 years both domestically and globally. He serves on CMRI's Finance & Investment Committee and the Audit & Risk Committee.

Ms Fiona Crosbie

Ms Crosbie is a partner of the international law firm, Allens, where she leads the competition and consumer law practice and serves on the firm's board. She is also a member of the Competition and Consumer Committee of the Law Council of Australia. She chairs CMRI's Audit & Risk Committee.
ELIZABETH

Elizabeth seemed to have constant sinus infections and her mum, Natasha, knew something was wrong, even though blood tests showed nothing. In July 2012, when Elizabeth was just 5 ½ years old, she had double vision and her mum took her to hospital. Scans showed Elizabeth had a rhabdomyosarcoma (tumour) in the sinus area, eye orbit and intracranial extension.

“Elizabeth started emergency chemotherapy, along with 28 days of radiation, followed by weekly chemotherapy for one year,” her mum said. Surgery was not an option because of where the tumour was positioned. It was an aggressive tumour, and they caught it just in time, before it invaded her brain tissue. While the tumour became inactive, the optic nerve in her right eye was unable to be saved.

“We’re very supportive of basic research into cancer and want to do more to help CMRI.”
## Committees & Advisory Boards

### Finance & Investment Committee

The Finance and Investment Committee manages and monitors the performance of CMRI’s investment portfolio. Committee members include:

- Mr Rod Atfield (Chair, retired February 2016)
- Prof. Frank Martin
- Mrs Carolyn Forster
- Jeremy Waine (Chair, March 2016)
- Prof. Roger Reddel
- Mr Ralph Mitchell
- Mr Bruce Fink
- Mr Michael Loughman
- Mr Paul Scully
- Dr Don Stammer

### Audit & Risk Committee

The role of the Audit & Risk Committee is to assist the CMRI Board with financial reporting practices and provide advice on operations and risk management strategies. Committee members include:

- Mr Rod Atfield (Chair, retired February 2016)
- Prof. Frank Martin
- Mrs Carolyn Forster
- Ms Fiona Crosbie (Chair, March 2016)
- Mr Jeremy Waine
- Mr Bruce Fink
- Mr Michael Loughman
- Mr Aleks Lupul (April 2016)

### Building Foundation Executive

A sub-committee of the Board advising it on fundraising for the redevelopment of CMRI’s building and assisting in fundraising efforts. Members include:

- Mrs Carolyn Forster (Chair)
- Prof Frank Martin
- Mr Albert Wong
- Mr Bruce Fink
- Ms Virginia Judge (Deputy Chair)

### IP (Intellectual Property) Committee

The role of the IP Committee is to provide strategic advice on CMRI policy and management of intellectual property. Committee members include:

- Prof. Graeme Stewart (Chair)
- Prof. Ian Caterson (retired March 2016)
- Prof. Frank Martin
- Mr Rod Atfield (retired February 2016)
- Mr John Dunlop

### Nominations & Remuneration Committee

The Nominations & Remuneration Committee assists the Board on Board and Committee appointment practices, succession planning and performance evaluation processes. Committee members include:

- Prof. Frank Martin (Chair)
- Mrs Carolyn Forster
- Mr Rod Atfield (retired Feb 2016)
- Mr John Dunlop

### Research Excellence Foundation

Founded by Mr Huang to reward and encourage excellent research by CMRI Scientists.

- Mr Xiangmao Huang (Chair)
- Prof. Roger Reddel

### Judging Panel for Research Excellence Awards

- Prof. Suzanne Cory
- Prof. Merlin Crossley
- Prof. Emma Whitelaw
- Prof. Brandon Wainwright

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Thank You Rod Atfield

Rod Atfield is taking a step back from his responsibilities with Children's Medical Research Institute, retiring from the board after 16 years. Mr Atfield made what he describes as a very difficult decision, to retire, after concluding it was time to allow freshly recruited board members with similar abilities to be given the wonderful opportunities he had enjoyed during his many years with CMRI.

“...I am in awe of the quality of work that is achieved. The recognitions our scientists have received show just how well they are perceived by their peers,” Mr Atfield said.

It was that recognition that attracted Mr Atfield to CMRI. Through the years, he says he’s seen the Institute change for the better. “We have recruited outstanding scientists, and we have expanded the labs through the building development, giving a number of highly skilled scientists the opportunity to run their own labs, resulting in greater results. In the fundraising area, which substantially relied on Jeans for Genes, we’ve now grown with the Great Cycle Challenge.”

Upon reflection, Mr Atfield believes he has achieved many great things at CMRI. But he says his most proud achievements were in investment, particularly in helping the Institute through tough times, such as the global financial crisis.

Mr Atfield’s future is looking bright. As he approaches his 79th year, he’s hoping to travel more with his wife, both nationally and internationally, and continue to enjoy his grandchildren.

Mr Rodney Atfield
Children’s Medical Research Institute is committed to ensuring the health, safety and welfare of its workers and visitors. Workers include all staff members, students, contractors and visitors.

A medical research institute like ours has many hazards that need to be managed to keep our workers safe. We have a comprehensive WHS plan and risk management framework that enables us to manage WHS in an efficient and effective manner.

CMRI undertakes the following yearly worker training: General WHS; Emergency and Evacuation; Biological and Chemical Safety; Radiation Safety; and Ergonomics. These topics are covered by a face-to-face seminar, along with follow up online quizzes. Our emergency wardens also undergo additional training as required by Australian standards. In 2015, the training series was streamlined with our expert trainers condensing seminars to allow for the best balance of sharing of safety information versus the time it takes to deliver.

CMRI has completed many initiatives during the year to support WHS training and management. In 2015, a fully online electronics visitor/contractor check-in system was put in place. This allows much better tracking of visitors and a holistic view of contractor visits. The system also allows staff to check-in after hours, with a video screen showing other staff who is on site. A contractor induction policy has been written and electronic inductions will be implemented in 2016.

The implementation of an electronic learning system for safety training has seen an increase in staff completing safety training to a very high level (> 85%). The MindFlash system we use allows staff to undertake their safety training at their desktop computer or on their own electronic device of choice. Institute research and administration groups are continuing to put their safety training documents into these central systems provided by the Institute.

CMRI has a comprehensive online incident reporting system where workers are required to report all safety incidents and near-misses. Management review of incidents and near-misses enable us to continually improve our work environment so it can be as safe as practicable. Bi-annual workplace safety checks are also undertaken, with any required remediation carried out as soon as practicable.

The highest number of reported incidents continue to be of an ergonomic nature. CMRI takes a personal approach to ergonomics, and we provide tailored solutions to each staff member who raises a concern.

CMRI takes pride in the safety culture it harbours. We remind all workers at induction and at our General WHS training:

\[ \text{Mind on Task} \Rightarrow \text{Eyes on Task} \Rightarrow \text{Safe Outcome} \]

Gender Equality

Each year, CMRI submits an annual public report with the Workplace Gender Equality Agency in accordance with the requirements of the Workplace Gender Equality Act 2012 (WGE). CMRI has a long history of encouraging female researchers, and today 58% of our scientists are women. In fact, 67% of all CMRI staff are female. Managers include an almost even mix of more women (16) than men (11). Four of our eleven research leaders (36%) are women. CMRI introduced a gender equality committee in 2014 to find ways to encourage more women into senior research leadership roles.

Thank you to the Australian community and our research, business and corporate partners for their ongoing support. With their help, we can continue to advance the prevention and treatment of disease and create a healthier, brighter future for all children.