CMRI 2013 Annual Report

Energised

Healthier kids, brighter futures
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Find new and better treatments that could benefit most types of cancer
See that our epilepsy treatments help children (and adults) around the world

New treatments for infectious diseases

Gene therapy cures for rare genetic diseases in children

Telomere research to help us understand predisposition to disease

Develop new treatments for kidney disease

DNA is packaged into chromosomes and holds the key to finding cures for childhood diseases
10 of the researchers at CMRI have been here 20 years or more.

20 are PhD students newly arrived or here for a few years only.
Children’s Medical Research Institute (CMRI) was Australia’s first dedicated paediatric medical research facility and has been helping to save the lives of children for over 55 years.

You could call us the “oldest” such institute, but we prefer to think of ourselves as “55 years young”.

Our research teams, areas and projects have changed and progressed over the decades so that we continue to remain at the forefront of international, cutting-edge research into treatment, prevention and cures for cancer, epilepsy, birth defects and genetic diseases.

Some of CMRI’s current research teams have been working hard for over 20 years, while others are newly established. In every case, the researchers and team leaders in each lab carry the enthusiasm and energy of youth. Whether they are a sixty-year-old whose eyes still light up with a theory to test, a fast-talking thirty-year-old with a recent string of successes under their belt, or a passionate twenty-something PhD student just learning the ropes, their bright ideas keep coming. Together, they are accelerating our fight against childhood diseases.

This combination of people, experience and energy is working hard to seize today’s opportunities. These include:

> A New Building… The Stage 1 Redevelopment of our facilities is nearly complete. This infrastructure will almost double our research capacity and speed up discoveries.

> New Tools… Thanks to generous funding from ACRF and other sources, CMRI now has technology and expertise found nowhere else in Australia and in some cases nowhere else in the world.

> New Ideas… We’ve expanded our research teams to include four new groups with new ideas who are focussing on and expanding our strongest research areas, including cancer, embryology and neurobiology.

This year we highlight the hard-thinking and hard-working members of our research teams and their amazing ideas. We also invite you to join the greater CMRI team that is cycling, wearing jeans, or hosting fundraising events to help create a brighter future for children everywhere.

Welcome to our annual report for the calendar year, January through December, 2013.
However, Phase 1 will remain ‘near’ completion for some time as we seek an additional $8 million to complete the fit out of the interior laboratory spaces. It is for this reason I have become a member of the Capital Foundation sub-committee of CMRI’s Board.

CMRI recognises that many of our current supporters prefer to have their funds directed to CMRI’s ongoing research programs, and we agree that it is crucial to maintain and even increase funding for laboratory work. Nevertheless, it is equally important that we provide better infrastructure for that important work and create new opportunities to expand those research programs in ways currently not possible.

Thus, I and fellow members of the Capital Foundation, which is chaired by our Vice-President, Mrs Carolyn Forster, believe we must also pursue support for the redevelopment of our building. To this end, the Capital Foundation will work to find new supporters interested in helping with this vital goal.

Mr Huang of YuHu Group has already demonstrated his commitment to the redevelopment with a significant donation of $1 million. We believe there are more visionary people like Mr Huang in the community, and we will be seeking them out in the years ahead so that not only Phase 1 can be completed, but Phases 2 through 5 as well.

I am, as ever, proud of our scientists and the world-leading research they produce. I know we are making a significant impact on medical research worldwide, which will be hugely instrumental in bringing new and better treatments to children for generations to come.

I am also happy to report that the economic downturn which so severely affected our income streams for many years has ceased its downward trend, and our investments are regaining the value that they lost in previous years. Our recent restructuring of Fundraising has reduced costs in many areas, while simultaneously expanding efforts. Support for Jeans for Genes in its 20th year continued to be strong. In addition, there was also tremendous support for our new initiative, the Great Cycle Challenge. This inaugural event raised over $1 million for our cancer research programs, and we hope to repeat this success in 2014.

Our prized Committees, some as old as CMRI itself, were imaginative and energetic in their efforts and made major contributions this year as well. We thank them and all who donated their time, money and creativity in support of CMRI.

This fundraising income was especially crucial as government support for research projects declined in 2013. CMRI researchers fared better than the national average, a positive reflection on their skill, but many were nevertheless affected by cuts or restructuring of NHMRC and ARC funding.

Also important to our research efforts is our continued collaboration with both the Westmead Research Hub partners (The Children’s Hospital at Westmead, Westmead Hospital, Westmead Millennium Institute, and Kids Research Institute) and the Kids Cancer Alliance (which includes Sydney Children’s Hospitals Network, Hunter Regional Hospital, and Children’s Cancer Institute). These collaborations provide invaluable access to high-tech equipment and sharing of expertise between researchers to advance all of our vital programs.

I would like to end by thanking our Board members for their generous service. There were several notable resignations in 2013. Professor Kathryn North moved on to a position in Melbourne, and John Bevins retired early in the year. John Dunlop, who has been a Board member for an amazing 43 years, resigned in October, but cannot commit to full retirement and has joined our Nominations & Remunerations Committee. John Dunlop is featured on page 56 of this report.

Although we miss the valued colleagues who have retired, we have enjoyed welcoming new Board members including Mr Bruce Fink, Mr Michael Loughman, Ms Fiona Crosbie, Dr Luciano Dalla-Pozza, and Mr Albert Wong. They all bring valuable skills to CMRI, and we welcome their contributions and enthusiasm as we work together to build the infrastructure needed to see CMRI create an even brighter future for children’s health.

Welcome to CMRI’s annual report for 2013, and I hope you will join us in our ongoing efforts to re-vitalise CMRI. Together we can achieve our goal of treating or preventing serious childhood diseases, and we can also make CMRI ready to face the medical research needs of the next generations.

Frank Martin
President, May 2014
Report from the Director

2013 has been a landmark year for CMRI. Our researchers have made notable advances in each of our four core areas of cancer, embryology, nerve cell signalling, and gene therapy. At the same time, every one of our departments has been working very hard to prepare for a greatly expanded research effort.

CMRI’s research programs are designed for long-term impact. The research questions we pursue are designed to increase our understanding of the fundamental biological processes underpinning health and normal development, and of what goes wrong in specific diseases. It is this knowledge which can be “translated” into major advances in children’s health through better treatments and prevention strategies.

We also use short-term measures of research performance and impact to monitor our progress. One of these is citation analysis - the number of times a researcher’s work is acknowledged by other researchers. By such measures Australian research overall does very well, with an impact 65% above the world average, and Australia’s independent medical research institutes (MRIs) do even better. In terms of citations per publication, CMRI research continues to rank among the very top Australian MRIs.

CMRI is committed to continually increasing the impact of its work on childhood diseases, and 2013 has been a very significant year for CMRI in all aspects of its preparation for a greatly expanded role in paediatric medical research. Our strategy is to increase the strength and depth of the already highly successful research programs which have been built up over several decades, by forming clusters of Research Units in each of our key research areas. As a first step, we have created four Research Groups, led by talented researchers: Hilda Pickett (Telomere Length Regulation), Tony Cesare (Genome Integrity), Mark Graham (Protein Biochemistry), and Robyn Jamieson (Eye Genetics). Tony Cesare was recruited from the Salk Institute (California, USA) and the other appointments are internal, formally recognising leadership that has been displayed over considerable periods of time.

Over the years ahead, we will continue to recruit leading biomedical scientists to establish research groups at CMRI which will complement and strengthen our research programs. Additional laboratory space is therefore essential. Under the leadership of our Head of Building Redevelopment, Greg Craig, and supported by a $20 million grant from the NSW Government, building work commenced early in 2013. Stage One of the redevelopment will deliver urgently needed space to house our specialist research facilities, especially the Bioinformatics Unit, the Biomedical Proteomics facility (including the Australian Cancer Research Foundation [ACRF] Centre for Kinomics), and the ACRF Telomere Analysis Centre (ATAC), as well as laboratory space for new groups.

Our Finance Department, led by Chief Financial Officer, Ralph Mitchell, and our Operations Department, led by Darryn Capes-Davis, have continued to improve the financial and operating systems that will underpin our expanded research. Our aim is to continually refine our systems, such as Workplace Health and Safety, so that they are not only exemplary in every regard, but also impose the minimum possible compliance burden on our staff. Our aspiration is to fund a considerable portion of CMRI’s future work through financial returns from work that is being done now, so considerable effort is being made by our CFO, our Intellectual Property Committee, BioLink Australia, and our researchers to identify and protect research of future commercial value.

Fundraising is also a critically important aspect of CMRI’s activities. We would not be able to pursue long-range, high-impact research programs without it. CMRI was very fortunate to have Lyndsey Rice as Acting Head of Fundraising, in a maternity leave replacement role for Laura Edwards, for much of 2013. Our existing fundraising activities, including Jeans for Genes, remained strong, and the Great Cycle Challenge was a very successful addition. This work, and many other aspects of our activities are underpinned by Marketing and Communication, led by Lorel Colgin. As always, we greatly appreciate the ongoing efforts of our tireless Fundraising Committees and all who raise and contribute funds generously to allow our work to continue. Fundraising for our building development, led by Virginia Judge and CMRI’s newly established Capital Foundation, is also essential for our future.

About one third of CMRI’s revenue comes from competitive, peer-reviewed grants. The success rate of our applications to the National Health and Medical Research Council was double the national average in 2013, which reflects the excellence of CMRI’s research, but competition for this increasingly limited pool of funding increases every year. We greatly value continued significant funding from Cancer Council NSW, Cancer Institute NSW, Cure Cancer Australia Foundation/Cancer Australia, and many other funding agencies. During this year, ACRF awarded a $2 million grant for the Telomere Analysis Centre.

We continue to value our many external partnerships. Our international collaborations are highlighted in this annual report. Our long-standing key relationship with Children’s Hospital Westmead has been enhanced by the Kids Cancer Alliance, a collaborative effort involving CMRI, Sydney Children’s Hospital Network, Children’s Cancer Institute, University of Sydney, University of NSW, and others – encompassing almost all paediatric cancer clinicians and researchers in NSW. There are many exciting developments underway in the Westmead precinct, and we continue to share major research equipment and research activities in the Westmead Research Hub, enabling us to extract maximum value out of every dollar spent on research.

CMRI greatly appreciates the community’s ongoing support. We hope you enjoy reading our annual report for 2013, which highlights some of the achievements this support has enabled in our quest for major improvements in children’s health.

Roger Reddel

Lorimer Dods Professor and Director, May 2014
Research Report

In this section you’ll get to meet our research teams and learn more details about their exciting work.
CMRI has always tackled difficult problems and succeeded. Now we are taking on some of the most pressing diseases affecting Australian children and many children worldwide:

Barring accidents, congenital abnormalities and genetic disorders are the leading causes of death in children aged 0-4.

Barring accidents, cancer is the leading cause of death in children aged 4-14.

CMRI researchers are facing these challenges head on. You’ll see that basic research is a powerful approach to finding answers for a wide range of diseases. We have world-leading researchers and relative newcomers, all with bright ideas, the right skills, and the energy and enthusiasm to get us where we need to go.
CMRI’s Collaborations

Asia
> Biosignal Research Center, Kobe University, Japan
> Genome Institute of Singapore, Singapore
> Nanyang Technical University, Singapore
> University of Hong Kong, Hong Kong

Australia and New Zealand
> Baker IDI Heart and Diabetes Institute, Melbourne VIC
> Biomolecular Frontiers CoRE & ARC Centre of Excellence in Bioinformatics, Macquarie University, Sydney NSW
> Calvary Mater, Newcastle NSW
> Centenary Institute, University of Sydney NSW
> Children’s Cancer Institute Australia, Kensington NSW
> Clinical Geneticists & Ophthalmologists throughout Australia and New Zealand
> CSIRO Division of Health Sciences and Nutrition, Parkville VIC
> CSIRO Materials Science & Engineering, Parkville VIC
> Diamantina Institute, Centre for Immunology and Cancer Research, University of Queensland, Brisbane QLD
> Dunedin School of Medicine, University of Otago, New Zealand
> Institute for Molecular Biosciences, University of Queensland, Brisbane QLD
> John Hunter Hospital, Newcastle NSW
> Kids Research Institute, Westmead NSW
> Kolling Institute of Medical Research, St Leonards NSW
> Ludwig Institute for Cancer Research, Melbourne VIC
> Massey University, New Zealand
> Mental Health Research Institute, Parkville VIC
> Monash University, Melbourne VIC
> Murdoch Children’s Research Institute, Melbourne VIC
> Northern Cancer Institute (HRW), North Shore Private Hospital, St Leonards NSW
> Peter MacCallum Cancer Centre, East Melbourne VIC
> Queensland Brain Institute, Brisbane, QLD
> Queensland Institute of Medical Research, Herston QLD
> Royal North Shore Hospital, St Leonards NSW
> Save Sight Institute, University of Sydney, Sydney NSW
> School of Medical and Molecular Biosciences, University of Technology, Sydney NSW
> St Vincent’s Institute of Medical Research, Melbourne VIC
> Sydney Adventist Hospital, Wahroonga NSW
> The Children’s Hospital at Westmead, Westmead NSW
> The Royal Melbourne Hospital, Parkville VIC
> University of Auckland, New Zealand
> University of Melbourne, Parkville VIC
> University of New South Wales, Sydney NSW
> University of Newcastle, Newcastle NSW
> University of Otago, Dunedin, New Zealand
> University of Queensland, Brisbane QLD
> University of Sydney, Sydney NSW
> University of Wollongong, Wollongong NSW
> Victor Chang Cardiac Research Institute, Darlinghurst NSW
> Walter and Eliza Hall Institute, Melbourne VIC
> Westmead Millennium Institute, Westmead NSW
Europe

> Centre Hospitalier Universitaire Vaudois and University of Lausanne, Switzerland
> Centre National de la Recherche Scientifique, Toulouse, France
> European Collection of Cell Cultures (ECACC)
> Freie Universität, Berlin, Germany
> Great Ormond Street Hospital, London, UK
> Heinrich-Pette-Institute, Hamburg, Germany
> Hospital Henri Mondor, Paris, France
> Institut Curie, Paris, France
> Institute of Developmental Biology and Cancer, Nice, France
> Max Planck Institute for Biochemistry, Germany
> Medical University of Vienna, Vienna, Austria
> MRC National Institute for Medical Research, London, UK
> National Cancer Institute, Italy
> Necker Hospital for Sick Children, Paris, France
> University Hospital Göttingen, Göttingen, Germany
> University of Canterbury, Kent, UK
> University of Edinburgh, Edinburgh, UK
> University of Frankfurt, Frankfurt, Germany
> University of Groningen, Groningen, The Netherlands
> University of Heidelberg, Heidelberg, Germany
> University of Liverpool, Liverpool, UK
> University of Southern Denmark, Odense, Denmark

North America

> Albert Einstein Medical Centre, Philadelphia PA, USA
> Capital Biosciences Incorporated, USA
> Harvard Medical School, Boston, MA USA
> Institute of Cancer Genetics, Columbia University College of Physicians and Surgeons, New York NY, USA
> Massachusetts General Hospital, Boston MA, USA
> MD Anderson Cancer Center, University of Texas, Houston TX, USA
> National Institute of Allergy and Infectious Diseases (NIAID), Bethesda MD, USA
> National Institute of Child Health and Development, National Institutes of Health, Bethesda MD, USA
> Terry Fox Laboratory, BC Cancer Agency, Vancouver BC, Canada
> University of Massachusetts, Boston MA, USA
> University of Washington, Seattle WA, USA
> Wake Forest University, Wake Forest NC, USA
The Cancer Research Unit investigates telomeres, which are important for senescence (aging) and all cancers. Our main emphasis at present is on understanding how cancer cells continue to proliferate using the Alternative Lengthening of Telomeres (ALT) mechanism. Better understanding of this mechanism will enable us to develop better treatments against ALT cancers, which are some of the most aggressive types, including glioblastoma brain tumours and osteosarcoma.

**Research Update**

We seek to understand the immortalisation of cancer cells (i.e. their ability to divide indefinitely) and how this might be counteracted to develop new anti-cancer therapies. We know that maintenance of telomeres is essential for unlimited cell division. Telomeres are DNA sequences that act as protective caps at the ends of chromosomes. Each time a cell divides, telomere DNA is lost and this serves as a “clock” limiting the cell’s ability to reproduce. When telomeres shorten, senescence is triggered and cells stop dividing. Immortal cancer cells are able to add back telomere DNA to overcome telomere shortening and prevent senescence. They do this using either an enzyme called telomerase or by using an Alternative Lengthening of Telomeres (ALT) mechanism.

Now, with a better idea of some of the genes involved in ALT, we are working hard to understand the mechanism. How is ALT switched on and how it is regulated in cancers? Understanding this will allow us to find weaknesses that will be the target of new cancer therapies. For example, we know that loss of the ATRX gene’s function contributes to ALT activation, but we have yet to determine why this is the case and exactly what ATRX is doing in ALT. Other genes under investigation by our lab are the CST complex, as well as the role of p53 in ALT activation.

APBs are nuclear structures found in ALT cells, but large APBs are also associated with cell senescence. Senescence is when cells cease dividing but continue to function. We are dissecting the pathways of protein interactions and genetic regulation that lead to formation of these large APBs. Once we understand this pathway, we may be able to selectively induce senescence in ALT cells. This would prevent further growth of ALT cancers. We suspect that ALT cells are particularly susceptible to senescence, as we often find that 4-5% of ALT cells in culture are senescent, so they are most likely generated at a higher rate than in telomerase-positive cancer cells.
In collaboration with Dr Loretta Lau of The Children’s Hospital at Westmead, we are looking at rare neuroblastoma tumours that have no telomere maintenance mechanism (TMM)—neither ALT nor telomerase. Malignant tumours usually need to be immortal because they need the capacity to reproduce in vast numbers in order to grow large enough to be life-threatening and to accumulate the genetic mutations required for metastasis and other higher stage tumour characteristics. However, we predicted that in the case of paediatric cancers, where the cancer cells have long telomeres to start with, there may be no need to activate a telomere maintenance mechanism and become immortalised. The existing telomere lengths would be sufficient to produce a dangerous tumour. Our work with Dr Lau has now identified such tumours, specifically some neuroblastomas. Because they lack a TMM, these tumours should be biologically different and have a different prognosis.

Finally, we are analysing telomere lengths of children undergoing cancer treatment to determine clinical outcomes. We are investigating whether telomere length predicts acute toxicity reactions to chemotherapy, toxicity reactions that persist or occur long after treatment has stopped, and the success of bone marrow transplants. Maybe this will be one of the factors clinicians need to take into account when they are tailoring each individual patient’s treatment.

Normal cells in our body lose some telomere DNA each time they reproduce. This leads to aging or “senescence” where the cells eventually stop growing. Cancer cells, in contrast, add back telomere DNA so they can keep growing out of control to form a tumour.
The Telomere Length Regulation Group focuses on understanding the molecular mechanisms underlying telomere length regulation and how telomere length can be manipulated to control cell division.

**Research Update**

**Telomeres**
Telomere length regulation involves an intricate balance between lengthening and shortening processes, which ultimately determines the capacity of a cell to divide. Telomere length dysregulation can result in cancer, or in an emerging spectrum of premature aging disorders. We are investigating the mechanism of telomere rapid deletion by telomere trimming, how telomerase variants confer cancer risk, and how sequence content contributes to telomere structure and function. This research will underpin further clinical studies, and will impact upon cancer control and the treatment of short telomere syndromes.

**Telomere trimming**
Telomere trimming rapidly deletes long telomere DNA and functions to prevent the persistence of over-lengthened telomeres and appears to be a normal, well-regulated process. We have identified telomere trimming in normal human cells of both germline and somatic origin and are currently investigating telomere trimming in other cells. In addition, we are characterising the proteins and cell signalling pathways that regulate telomere trimming.

**Characterisation of the TERT locus**
TERT is one of two genes found in a portion of chromosome 5 which is associated with risk of many cancer types. TERT encodes a key activity of telomerase. Telomerase is responsible for maintaining telomere lengths in the germ line, in rapidly dividing cells like the bone marrow, and is also activated in 85% of all cancers. Studies have identified numerous single nucleotide polymorphisms (SNPs, i.e. genetic variations commonly found in the population) within the TERT gene that are associated with risk of serious epithelial ovarian cancer and breast cancer. We are investigating the role of cancer-associated SNPs in telomerase activation during cell immortalisation, which is important for cancer.

**Telomere sequence content**
Telomeres are thought to be comprised almost exclusively of DNA with the code ‘TTAGGG’ repeated over and over. We have used whole genome sequencing to demonstrate that telomeres also contain substantial amounts of variant repeat sequences that are generated in cells using either telomerase or Alternative Lengthening of Telomeres (ALT). Variant repeats display different protein binding capabilities compared to the normal repeat sequence. We are investigating variant repeat content, the mechanisms of variant repeat generation, and how variant repeats impact upon binding of regulatory and other proteins to telomere DNA and how this affects the many functions of the telomere.
“All our science, measured against reality, is primitive and childlike—and yet it is the most precious thing we have.”

— Albert Einstein
Research in the Cell Biology Unit 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 biological and biochemical properties of telomerase in order to rationally design better anti-cancer treatments.

**Research Report**

**Telomeres and Telomerase**

A dynamic feature of telomeres is that they shorten during every cycle of DNA replication and cell division. When telomeres have shortened sufficiently, the cellular senescence program is activated, resulting in permanent withdrawal from the cell cycle. Telomere shortening is a powerful and essential tumour suppressor mechanism.

Telomerase is a protein complex that is able to add back telomere DNA and counteract the normal shortening process. By producing abnormally high levels of telomerase, cancer cells are able to avoid telomere shortening and thus bypass senescence, thereby becoming immortal. *Telomerase is expressed in >85% of all human cancers and is considered a prime target for anticancer therapeutics through the development of telomerase inhibitors.*

Our research projects are directed at understanding the properties of the telomerase enzyme at the cellular and biochemical level. This includes studying the association of telomerase with its DNA substrate, active recruitment of telomerase to the telomere, telomerase enzymology, and structure, all with the long-term aim of using this knowledge to rationally design small-molecule inhibitors of telomerase as potential anti-cancer therapeutics. Much of our research is enabled by our ability to produce human telomerase on a large scale.

**Telomerase structure**

In collaboration with Dr Scott Cohen at CMRI and Professor Michael Parker at St. Vincent’s Institute (Melbourne), we aim to determine the atomic-resolution 3-D structure of the telomerase enzyme complex. An atomic-level structure will provide a template for rational and custom-designed small-molecule inhibitors of telomerase as potential anti-cancer therapeutics. The primary method for atomic-level structure
is X-ray crystallography. Despite the progress we have made with our over-expression system, we are as yet unable to generate the milligram quantities of enzyme necessary for crystallisation trials. Thus, the over-expression system remains an active area of research.

Telomerase association with its DNA substrate

Interfering with the ability of telomerase to bind telomeres provides a potential avenue for telomerase inhibition, through either direct inhibition of the enzyme, or indirectly through sequestration of its telomeric substrate. Telomeric DNA, owing to its repetitive G-rich sequence (TTAGGG), has the ability to form a compact folded structure called a G-quadruplex.

We work extensively with small-molecule ligands that specifically stabilise G-quadruplexes. In collaboration with Dr Jennifer Beck in the School of Chemistry at the University of Wollongong, we aim to evaluate ligands that may be specific for a particular conformation of G-quadruplex. Such compounds are also a valuable tool for looking at G-quadruplexes at the cellular level. Our guiding hypothesis is that different conformations of G-quadruplex will perform distinct functions at the telomere.

Recruitment of telomerase to the telomere

If telomerase cannot reach the telomere, it cannot bind or add back telomere DNA. There are many proteins involved in moving telomerase and we’ve found that TCAB1 is crucial. This work is helping us better understand telomerase movement in the cell and provides new targets for potential anti-cancer therapies.

Enzymology of telomerase and disease-associated mutants

We make use of disease-associated mutants of telomerase as a guide in identifying regions or even specific amino acids important for telomerase activity. Dyskeratosis congenita (DC) is an X-linked genetic disorder categorised as a premature ageing syndrome. DC is characterised by reduced proliferative capacity of certain tissues; notably, most patients die of bone marrow failure. At the molecular level, DC is a disease of insufficient telomere maintenance, and at least one hundred mutations in telomerase genes (hTERT, hTR, or dyskerin) have been identified that result in either reduced levels of telomerase or an enzyme with compromised activity. Thus, these mutations serve as a guide for understanding the mechanism at the molecular level.

A G-quadruplex is a special DNA structure that looks very different from the well known double helix. G-quadruplexes can form at the ends of chromosomes and may be an important target for cancer therapies.
The Genome Integrity Group studies fundamental causes of cancer and aging. We seek to understand how our genome (the set of instructions guiding cellular function) is protected from damage and how, when this protection fails, a disease like cancer may result. 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 tumour formation.

The critical leap in the understanding of telomere biology was our discovery that telomere protection and deprotection during the normal course of cellular ageing progresses through three distinct stages. In young cells with long telomeres, chromosome ends are arranged into a protective “closed-state” structure that hides the chromosome end away from the DNA damage response machinery. As telomeres shorten, the capacity to form this protective state diminishes, and some chromosome ends become exposed as “intermediate-state” telomeres. This stimulates the DNA damage response, meaning the cells see the telomere as “damaged” and in need of repair. However, retention of the telomere protein, TRF2, at intermediate-state telomeres prevents completion of this damage response and prevents end-to-end fusion of chromosomes.

Diseases Impacted by Our Research: Cancer, Aging

Research Report

Our long-term goal is to understand the fundamental mechanisms used by human cells to maintain genome integrity and how failures in these processes contribute to human disease. Currently we are using our expertise in the field of telomere biology to study specifically how changes in telomere structure relate to cell growth arrest in healthy cells and, conversely, how changes in telomere structure cooperate with the loss of tumour suppressors to promote genomic instability and cancer. As our research base and technical capacity grows, we anticipate using our ability to modulate telomere biology as a model to study fundamental mechanisms of genome protection in human cells.
The greatest single achievement of nature to date was surely the invention of the molecule DNA. The capacity to blunder slightly is the real marvel of DNA. Without this special attribute, we would still be anaerobic bacteria and there would be no music.

— Lewis Thomas

Our recent discoveries have centred on understanding the role of intermediate-state telomeres in human telomere biology. Prior to our discovery of intermediate-state telomeres it was thought that chromosome ends adopted either a protected or unprotected state. What we can now surmise is that the unique properties of intermediate-state provide telomeres with their tumour-suppressive and genome protective qualities.

Now that we understand the presence of the critical intermediate-state of telomere deprotection we can begin to establish the molecular framework underlying the telomere-dependent phenomena of cellular ageing, tumour suppression and genomic instability.

Our current research expands on these discoveries as follows:

Deciphering the kinomics of the telomere deprotection response

The observation of differential ATM activity induced by intermediate-state telomeres was an exciting and surprising finding. We are now working with the ACRF Centre for Kinomics at CMRI to understand how spontaneous telomere deprotection is signalled in cancer cells, how differential ATM activation in response to intermediate-state telomeres is regulated and which downstream ATM pathways are upregulated in response to intermediate-state telomeres.

Understanding the telomere deprotection response in the context of the cell cycle

Our observations of deprotected telomeres are consistent with epigenetic marks that are capable of being passed between cell cycles and across cell division to regulate growth arrest specifically in the G1-phase of the cell cycle. We are focusing on understanding the epigentic pathways that allow the passage of DNA damage response positive telomeres across mitosis, the effect deprotected telomeres have on cell division, and putative effects telomere deprotection may have on unexpected areas of cell biology.
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.

Unit Head:
Dr Megan Chircop, BSc (Hons) PhD

Research Update

Basic research: molecular mechanisms of mitosis (aka cell division)

The Cell Cycle Unit has already identified a dozen different CME (clathrin-mediated endocytosis) proteins involved in mitosis. Some of the major proteins we’re interested in are: SNX9, Dynamin II, Clathrin, Intersectin 2, and Calcenurin, the latter being a key regulator of endocytic proteins.

Despite the identification of many mitotic proteins, the molecular mechanisms driving mitotic progression and how these proteins cooperatively function to complete mitosis in mammalian cells is not fully understood. Our basic research currently focuses on the following key areas:

Understanding the mechanism of action of each of these CME proteins known to be important for mitosis.

Going beyond CME proteins to look at membrane trafficking at the site of cytokinesis. Golgi, ER, endosomes, etc. all traffic in a regulated and sequential manner in order to remove or deliver proteins required for abscission, the stage of cell division where the cells physically separate. Using fast time-lapse, super high-resolution microscopy, we are able to follow individual structures during cytokinesis.

Investigating the intracellular bridge allows us to better understand the tubular vesicle structures which are important for cytokinesis but whose function is unknown. We are using EM tomography to generate 3D morphological images of the intracellular bridge in order to study the structures there. We’ve found that if we deplete cholesterol, we lose the tubular vesicles at the bridge and prevent cytokinesis. We believe the cholesterol-rich membrane protein, GRAF1, may be tubulating these vesicles and this is currently under investigation.
Cell division errors increase the potential of a cell becoming cancerous. Thus, understanding this basic biological process underpins our understanding of cancer biology mechanisms, which can lead to the identification of targets for therapeutic anti-cancer drug design.

**Translational biology: drug discovery of new anti-mitotic compounds for cancer treatment**

We have discovered that a subset of endocytic proteins are required for mitotic progression. Two of these have been identified as anti-cancer drug targets, as their specific inhibitors exhibit cytotoxic and cell growth inhibitory properties. These are the foundation of our drug development program, which is providing promising results:

We found that the Dynol 34-2 compound reduces glioblastoma tumour volume in mice by 70%. This is proof of concept that dynamin-inhibitors could work as anti-cancer drugs.

We identified the apoptotic pathway by which Dynol 34-2 kills cancer cells, and the glioblastoma brain tumours that did not respond to Dynol 34-2 were found to be Bcl-2 resistant, making them resistant to apoptosis, thus explaining their survival.

A breast cancer model was used to test a Bcl-2 antagonist, and we found this antagonist made Dynol 34-2 more effective. Further testing needs to be done, but we believe a combined treatment approach using Dynamin inhibitors and Bcl-2 antagonists will increase the efficacy of this treatment for glioblastoma as well.

During cell division all the DNA, contained in chromosomes, is copied and separated into daughter cells. Cytokinesis is a small but crucial step in the process where the daughter cells physically separate into two.
The Cell Signalling Unit studies the detailed molecular mechanisms of how signals are sent from one cell to another in the body, with a focus on nerve cell signalling and developing new treatments for epilepsy and other neurological disorders, as well as using an understanding of dynamin and other signalling molecules to develop new treatments for a range of diseases.

**Research Update**

Our research covers three overlapping areas of study: basic science around nerve cell communication, mass spectrometry technology, and drug discovery and translation into the clinic.

**Advances in each area depend on one another.**

In the realm of basic science, we continue to investigate proteins essential for nerve cell transmission, like dynamin, clathrin and calcineurin, and how they function. For example, we gained a better understanding of dynamin splice variants that result in two different tails on the protein. We know one tail is needed for calcineurin recruitment and we now know the function of the other tail. There are also splice variants that change the middle section of the protein, and we’ve now discovered why and how they affect different properties of dynamin.

This basic research is aided by our developments in mass spectrometry and drug discovery, and in turn informs further advances in these technologies.

Our mass spectrometry technology allows analysis of phosphorylated proteins, key regulators in many biological processes, including nerve cell transmission. Our ability to study phosphorylated proteins using mass spectrometry has expanded exponentially, from 10-20 proteins at a time, to 200-300, and now to 20,000 at a time. Mass spectrometry has told us more about the activity in the synapses of nerve cells than we even knew to ask.

In 2013, we published a massive piece of work around our discovery of Dingo 4A compound and its potential for treating infectious diseases. We also published our work on pyrimidines. The pyrimidine research proved ineffective for clinical use but can nevertheless be useful for basic science research. Two of our stories were published in the top level journal, Nature Protocols. One of these on how to synthesize...
the PIT STOP compounds that can regulate clathrin, and the other on how to make Dingos and Dynols, which are dynamin inhibitors.

Our drug development program is in the process of identifying pre-clinical drug candidates to treat epilepsy, cancer and kidney disease. We may be in this phase for anywhere from 2 – 10 years because there are a lot of variables to work out, namely improving drug delivery, safety, and specificity. For example, we have highly soluble compounds to treat kidney disease that can be easily delivered into the body, but we find that they breakdown too quickly in animals before they provide any benefit. Therefore, we need to tweak their chemical structures so that we maintain their effectiveness and solubility but make them tough enough to survive in an animal or human long enough to do what they need to do to treat disease.
Protein Biochemistry Group

Diseases Impacted by Our Research: Epilepsy, Cancer, Autism, Alzheimer’s

Group Leader:
Mark Graham
BSc (Hons), PhD

In the Protein Biochemistry Group, we are focused on answering fundamental questions, such as how does the brain work? And at the same time asking how a disease state can upset brain function. This fundamental knowledge is then applied to identify new potential drug targets.

Research Update

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. Specific extra knowledge is required to know the best way to attack the problem. We need knowledge of what the disease-related protein does and which enzymes and binding partners influence the protein function. The Protein Biochemistry Group uses advanced technology to identify enzyme pathways and map interacting protein partners for disease-related proteins.

Diseases of neurotransmission

The synapse is the place where nerve cells meet and is centre stage for many brain diseases. Many disease related genes have been identified that code for proteins involved in neurotransmitter release, synapse morphology (shape) and synaptic plasticity (ability to adapt). A major focus of the Protein Biochemistry Group is the synaptic vesicle cycle proteins involved in disease.

Endocytosis in neurotransmission

Endocytosis is a fundamental process that occurs in all eukaryotic cells. Defects in endocytosis limit the ability of a cell to internalise molecules and properly respond to environmental cues. Defects in endocytosis also affect exocytosis and intracellular trafficking because these processes are reliant on the proper sorting of the exocytic machinery during endocytosis. This is particularly important in the brain where cyclic rounds exocytosis and endocytosis are required to maintain neurotransmission.
The most well understood mode of endocytosis is clathrin-mediated endocytosis (CME). CME involves the formation of a lattice-like clathrin coat over the budding vesicle. Clathrin assembly proteins are responsible for making vesicles of a consistent size and shape. We are focused on defining the molecular mechanism of events during assembly of the clathrin coat, including the signalling events mediated by post-translational modifications.

A better understanding of neurotransmission 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.

CME Proteins

AP180 and CALM are a major focus of our group. Both are clathrin assembly proteins. AP180 is only found in brain and forms small vesicles in the synapses of neurons. The mechanism of clathrin assembly by AP180 is not yet well understood. The gene for AP180 has been implicated in bipolar disorder.

CALM is found in all cells of the body where it is involved in receptor internalisation which has implications for both Alzheimer’s and leukaemia. The fusion of CALM and AF10 via chromosomal translocation causes an acute leukaemia. A better understanding of CALM function may lead to therapeutics that can better target and potentially prevent the aberrant functions of this fusion product.

Polymorphisms, or small variations, in the gene for CALM have been found in Alzheimer’s patients. CALM may have a role the clearance of amyloid plaques or the processing of amyloid precursor protein (APP). CALM is known to be involved in APP-trafficking, so it could contribute to Alzheimer’s by trafficking APP to where it can break down and eventually form plaques. Understanding how CALM works will allow us to achieve the ultimate goal of finding subtle ways to regulate endocytosis and modulate its function to treat these diseases. While finding treatments for adult diseases, like Alzheimer’s, is not CMRI’s core mission, these discoveries are a fortunate by-product of our work on childhood diseases and can potentially help many people suffering from neurodegenerative disorders.

Follow the phosphate

Post-translational modification, which is the addition of molecules to a protein after it has been made, often significantly changes protein function. Therefore, rather than directly targeting a disease-related protein with a drug, it is possible to change protein function by targeting the enzymes involved in protein post-translational modification. We study protein phosphorylation, since it is the most common post-translational modification. We measure changes to the level of phosphate on both individual proteins and sometimes thousands of proteins at once to determine normal phosphorylation signalling that occurs presynaptically during neurotransmission. Phospho-signalling directed at disease-related proteins is picked up in these screens. The phospho-signalling pathways can potentially be exploited as a targeted way to treat disease.

We have identified novel activity-dependent signalling to proteins involved in Alzheimer’s disease, autism and epilepsy. Our signalling network data also fills in a major gap in our fundamental knowledge of presynaptic neurotransmission and this is where we aim to add significantly to global efforts to model brain function.
Embryology Unit

Diseases Impacted by Our Research: Birth defects in early development, especially...

- Head development
- Cranio-facial abnormalities
- Cleft lip and palate
- Saethre-Chotzen syndrome
- High cholesterol and heart disease
- Genetic diseases of liver and pancreas

Unit Head:
Professor Patrick Tam
BSc(Hons) MPhil PhD CBiol EurProBiol FAA FSB, FRS,
Deputy Director CMRI, NHMRC Senior Principal Research Fellow

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.

Research Update

Intersection of transcriptional and signalling activity in development

Our genetic and embryological studies showed that for the head to develop correctly, it requires a stringent control of WNT signalling that is synergistically interacting with transcriptional activity regulated by the Lhx1 gene.

Lhx1 is crucial for head development and have two key functions: 1) tuning the level of WNT signalling by regulating the activity of genes that control the signalling pathway 2) guiding the movement of cells by enabling cell-cell recognition so that the right cells make it to the right position at the right time for the head to form. Timing of Lhx1 gene expression is crucial, as Lhx1 is needed at a very precise window of time in development, but if activated inappropriately later in life, it can cause cancers.

Another gene, Otx2, has been identified as a key control gene for Lhx1. Otx2 oversees head development by regulating Lhx1 activity and losing its activity leads to similar developmental defects. However, losing Otx2 activity later at other times of development affects neuron differentiation in the brain and eye formation, suggesting that this gene is re-deployed for other functions as the embryo develops.

Abnormal shape of head and face is a clinical feature of the Saethre-Chotzen syndrome, caused by errors in the TWIST1 gene, another regulator of gene activity. In the mouse models, we showed that loss of Twist1 affects specific elements of the craniofacial skeleton and the muscles of the face, eyes and jaws. In addition, losing Twist1 function in the limb causes malformations of the fingers and the bones in the wrist and forearm due to changes in signalling activity. We are now studying the genes that may be controlled by Twist1, which may provide a better understanding of the gene regulatory network of head and face formation.

An embryo develops from a single cell. Through cell division, the number of cells increase and then they begin to differentiate or change into the different types of cells needed for a fully functioning organism. Problems caused by gene mutations and environmental factors during these early stages can lead to severe birth defects.
Molecular control of gut development

We studied the role of the Rbm47 gene, which encodes an RNA binding protein in the cells lining the gut. Reduced function of this gene in mouse models disrupts the differentiation and the maturation of the gut cells. Rbm47 is essential for editing the messenger RNA to generate different versions of the template for making the proteins. We have shown that RBM47 is involved in editing the RNA encoding ApoB protein, which is essential for cholesterol transport. This is a newly discovered process that appears to be of fundamental importance.

We also identified several CDC42-related Rho GTPase that are active in the endoderm, the embryonic tissue that forms organs including the liver, pancreas and thyroid. We showed that these GTPases are required for proper cellular organization in the endoderm. Reduced gene activity results in abnormal modelling of the gut epithelium, which appears to be critical for cells to respond properly to signals from surrounding tissues. We are currently looking at the network of genes involved and how these GTPases interact functionally with each other.

Developmental function of Importin, a shuttle of protein into the nucleus

Importin 13 is a member of a large importin β superfamily of proteins that mediate the transport of proteins into the nucleus. Importin 13 (Imp13) function is closely linked to disease states such as X-linked mental retardation and childhood asthma and is implicated in development of the foetal lung, testis, brain and cornea. In contrast to other importins, full length (“L-”) Imp13 appears to have dual specific nuclear import and export roles; but it is not clear how it can mediate transport bi-directionally, what specific import or export sequences it recognises, and how this relates to the function of a novel testis-specific variant (“timp13”).

Our analysis of Imp13 mutant mice indicates that Imp13 is essential for early development, and nuclear transport and kinetic measurements in living cells imply that timp13 can inhibit nuclear import mediated by L-Imp13. We hypothesise that Imp13 targets a number of specific cargoes into/out of the nucleus that are critical to mammalian development, and that inhibition of nuclear import by the timp13 variant is an important counteracting mechanism. Our work, which is carried out in collaboration with Professor David Jans’ team at Monash University, aims to elucidate L-Imp13/timp13 function using a range of molecular cell biology, biochemistry and genetic approaches. We are also currently investigating the role of Importin’s ability to shuttle molecules between the cytoplasm and nucleus and implications for disease in the context of the nature of the cargo it is carrying in specific type of tissues.

Mouse embryo-derived stem cells for studying germ layer differentiation

We have derived a new type of stem cell from mouse embryos of different developmental stages of gastrulation. These cell types can renew themselves in culture, can differentiate (i.e. change) into cell types of multiple lineages, and are poised to differentiate. We have optimised the method to direct the differentiation of these cells into gut cells that specifically become liver and pancreas cells. The goal of the stem cell research is to establish the paradigm for treating inborn errors of metabolism using a combination of cell-based and gene therapies. This work is a collaboration with the Gene Therapy Unit in a joint effort with The Children’s Hospital at Westmead and CMRI.
Eye Genetics Group

Diseases Impacted by Our Research: Genetic eye disorders, including...

- Retinal disease
- Cataracts
- Glaucoma

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 causative disease genes are not yet known. We aim to discover the underlying disease genes and the functions of the proteins they encode.

Research Update

We use next-generation sequencing techniques and genomic investigations to pinpoint disease genes. The functions of the disease genes are investigated using cell, zebrafish and mouse model systems, which provide a passage to development of novel treatment strategies. The Eye Genetics Research Group uses whole genome approaches in human patients to identify underlying disease genes in eye and other developmental diseases. Cell based and animal model studies are undertaken to understand how the disease genes lead to the particular abnormality. These studies aim to open a window to further research for development of targeted treatment for these conditions.

Next-generation sequencing and genomics

There are 3 billion base pairs in the human genome, with 45 million of these base pairs found in the coding sequences of genes. Next-generation DNA sequencing is a powerful technology allowing examination of the coding sequences (exomes) of genes, or sequencing of the entire human genome. Many of the disease genes leading to blinding eye conditions such as retinal diseases, glaucoma and cataract are not yet known. The Eye Genetics Group is using high-resolution genomic techniques for novel disease gene identification in patients and families. A wealth of genetic data is obtained and our targeted bioinformatic approaches have led to identification of several novel disease genes.
Vision requires a complex coordination of many genes in order for the eye to develop and function properly. Just one gene ‘stepping out of line’ can cause blindness.

Understanding disease gene functions
We undertake investigation of the function of the novel disease genes we identify using cell-based, zebrafish and mouse model studies. Cell-based assays include those investigating the function of novel candidate disease genes which affect the polarity of lens cells. We are also analysing the function of candidate disease genes by examining the loss of their function in the zebrafish eye in a successful strategy we are undertaking in collaboration with researchers from the Brain and Mind Research Institute, University of Sydney. For more detailed understanding of disease gene function, we have demonstrated the impact of loss and abnormal function using the mouse as a model system.

Novel therapies in genetic eye disease
Our cell-based and animal model studies provide a platform for the exploration of novel therapies in genetic eye conditions including the use of gene therapy for retinal diseases and the role of stem cells in the eye.
The Gene Therapy Research Unit finds ways to correct genetic diseases in children. We are a joint initiative of Children’s Medical Research Institute and The Children’s Hospital at Westmead (CHW). Our primary goals are to develop more effective gene therapy methods and to translate basic research progress into improved health outcomes for children.

Unit Head:  
Professor Ian Alexander  
BMedSci MBBS (Hons) PhD FRACP (Paeds) CGHGSA,  
Director Laboratory Research and Senior Staff Specialist,  
The Children’s Hospital at Westmead (CHW), Professor in  
Paediatrics and Molecular Medicine, University of Sydney

**Diseases Impacted by Our Research:** All genetic diseases are potentially treatable by gene therapy, especially:

- SCIDX1 deficiency
- Bone marrow disorders
- Metabolic liver diseases

**Research Update**

**Clinical trials**

We have two clinical trials underway with The Children’s Hospital at Westmead: the SCIDX1 trial and MGMT trial. The SCIDX1 trial allows us to correct the SCIDX1 gene in patients with “boy in the bubble disease” and restore functioning of immune cells. The MGMT trial is aimed to improve the resilience of bone marrow in children with brain tumours who are undergoing chemotherapy. This allows them to withstand higher doses of chemotherapy with the aim of improving treatment of their cancer.

**Pre-clinical laboratory projects**

1. Gene therapy treatments for metabolic liver diseases.
2. Gene therapy for bone marrow disease, with the focus now primarily on immune deficiency.
3. Technological underpinnings of gene therapy. This research aims to improve vectors and technology for gene delivery into liver and bone.
4. Successfully trialled three life-long cures for inherited liver diseases in mice. We want to bring this treatment to the clinic as soon as possible and are now focussing on translating the techniques used in mice to humans.

**Focus on liver disease treatment research**

We studied mice with a liver disease that could be controlled by introduction of a small molecule into the mouse’s water, and we could control whether the liver was sick or not. Human hepatocytes (liver cells) were then grafted into the livers of these mice. These chimeras received either healthy or sick human liver cells obtained from the liver donation program. The sick liver cells consisted of urea cycle defects:
OTC-deficiency, ASL-deficiency, etc. We then treated these mice using gene therapy to validate the technique. In collaboration with colleagues at Stanford University in the US, we have validated a novel AAV capsid, a viral vector, which has real potential to treat human livers. There are still many hurdles to overcome to bring these treatments to the clinic but we hope to overcome them in the next few years.

Focus on vector and gene therapy technology research

In addition to the new AAV capsid for liver treatment, we are investigating ways to improve packaging of genes into AAV vectors, which are limited in size. One approach is using mini-promoters (DNA control codes needed for a gene to be read by the cell) to reduce the amount of DNA that needs to be packaged.

Gene therapy safety is critical, and we have projects aimed at increasing safety of treatments in liver and bone marrow.

We are also moving toward genome editing technology, which means correcting errors in the existing genes in a cell rather than introducing a new correct gene copy.

We want to expand our research and clinical grade vector capacity in order to reach a critical mass and take advantage of opportunities in this fast-moving field of gene therapy, where we are seeing real clinical benefits. As technologies improve, we will have even better prospects for treating genetic disease in the future.

Focus on challenges of childhood genetic disease

The neonatal liver is growing and presents very different challenges compared to the adult liver. For example, the AAV vector used to treat genetic liver disease does not integrate into the patient’s DNA; it is episomal. This makes the treatment safer, but it also means it is lost as the liver grows and the gene therapy benefits wear off over time, requiring re-delivery of the AAV treatment. We would like to avoid this need to repeat gene therapy treatments. We have published the best and most comprehensive analysis of AAV in developing mouse liver, and we are assisting other labs around the world in addressing the issues we have identified.

The AAV virus shown here can act like a miniature machine that carries a good copy of a gene into cells to replace a faulty copy and cure a genetic disease.
In the short term, we need to do experiments. And I need to train new people in my team to do them well. In the middle term, I need publications. These represent completed pieces of work that have withstood the scrutiny of international peer review and help us stay on track. And I don’t want to lose sight of the long-term vision. In 5 or 10 years, how can I make sure that this research achieves something really worthwhile?”

“Tackling these three tiers simultaneously is daunting — and exciting.”

“I enjoy being a lab head. I did as much post-doctoral work as I could; it was time to move on to new challenges. It’s invigorating. But as I mentioned, there are late nights. I just applied for $3 million in grants, am helping people write post-doc fellowships, and there’s big new projects and new avenues to pursue, and new research tools, cutting-edge technology like genome editing to master, all while trying to teach the basics to new staff. They’ll get it, but in the mean time I tend to take on all the risky experiments myself because I can quickly judge what’s working and what’s not.”

“I’m trying some big things. My mantra is ‘Go Big or Go Home’. We’re mapping DNA damage pathways, using live cell imaging to dynamically visualise telomeres and the DNA damage response, using genome editing to tag telomere and DNA repair proteins, and testing the in vitro results to see if they hold true in vivo.

“As well as trying to get the money to hire more people, because it’s too much for one human being to do.”

“Now I have a group of four, but I’m hoping to get more if the funding comes through. I could end up hiring as many as seven people if I win all the grants I’ve applied for, but that’s a lot like winning the lottery. Still, there’s that much work to do.

“I’ve been using conferences, networking and even social media (Twitter, Research Gate, Academia.edu) to actively find and pursue top talent. It’s an international competition to get the best. You can’t rely on the old methods of hoping someone reads your paper and is willing to come to you. If you want good, talented people you have to hunt them down.”

“I believe that if we do this right, in five years CMRI will be the top institute in the world to study telomeres. If researchers want to study in this field, they’ll come here.”

Talking about recruitment, when asked about how his family felt about being recruited halfway across the world, Tony says, “Moving two kids across an ocean with no family to help was an effort. If I can handle that, I can handle anything. Really, it was tough but no tougher than moving across the US would have been. There’s not been a lot of sleep this last year, but the kids have adjusted. They’re already using Aussie slang, like bikkies and slippery dip. I love ‘slippery dip’ for ‘slide’. They’ve even taken to the babycinno and are fully immersed in Sydney coffee culture.”

Tony has a lovely wife and two kids – Sam who turned 4 in May and Madeleine who turns 2 in October. While Australia is new to the toddlers, it’s not new to Tony and his wife, who were based in Sydney for several years during Tony’s first post-doctoral stint in Roger Reddel’s lab.

Researchers commonly study an additional three to six years after completing a Bachelor of Science degree to get their PhD. They then go on to do at least two, three-year stints as a post-doctoral fellow before having an opportunity to set up a lab of their own as Tony is now doing.

When asked if he wants his children to follow in his footsteps, Tony says, “I want them to be bankers! Seriously, I love science, but what I really want is for them to be happy, whether it’s doing science or something else.

“I enjoy being a scientist, and I enjoy being a dad. Sydney is a great place to be both. For the kids, it’s safe, sunny, with lots to do outside. We have lots of friends here; we probably know more people in Sydney than we do in the US. In terms of science, it has been incredibly pleasant to come back, be welcomed, and feel I can be successful here.

“I know at CMRI we are striving to do great telomere biology. It’s a collaborative, not a competitive environment. I’ve been in both, and I prefer being able to talk to senior management, bounce crazy ideas off them, and also learn from them how to run a lab. I feel supported at CMRI. I’m also very excited about ATAC.”

ATAC stands for the Australian Cancer Research Foundation Telomere Analysis Centre. The Centre will be established in CMRI’s new building, thanks to funding by the Australian Cancer Research Foundation. It brings together expertise and high-tech equipment in one place, where telomere researchers from around Australia working on cancer and aging and clinicians working on telomere diseases can go to advance their research.

“We’re on the cusp of something transformative,” Tony says. “In one year, I will have access to microscopy technology that is the envy of the telomere world. Now we’re in the ramp up phase, but soon we will see outcomes. We will be able to do anything we can imagine that current technology allows. We can mix it up with the world’s top researchers and do anything they can do. Putting all this telomere research skill in one place has great potential. It’s exciting to be part of an institute that’s growing and that has a real chance of achieving great things.”
Tony Cesare
Research Facilities & Services
In addition to accelerating research efforts within CMRI and the Westmead Research 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 an Australian first, the ACRF Centre for Kinomics, a joint venture with the University of Newcastle, which enables scientists to understand the master controls governing basic cell behaviour and develop new therapeutic drugs for a range of diseases.
Bioinformatics

Bioinformatics is the application of information technology to the study of biology and medicine. Modern molecular biology research uses a variety of techniques such as genomics (large scale sequencing of DNA) and proteomics (large scale identification and characterization of proteins by mass spectrometry) that generate vast volumes of data. Sophisticated computational techniques are needed in order for the data to be correctly acquired, stored, managed, visualized, analysed, and interpreted. Bioinformatics is essential to modern health and medical research and needs to be an integral component of every biological research group.

The CMRI Bioinformatics Unit is a research, training and service facility dedicated to meeting the bioinformatics and computational biology needs of CMRI staff and students. Under the leadership of Associate Professor Jonathan Arthur, the unit:

> coordinates bioinformatics activity within CMRI
> provides a professional support and development network for bioinformatics staff embedded in CMRI research groups
> collaborates with CMRI research groups on research projects with bioinformatics components
> provides training and education for laboratory-based research staff and students to develop computational biology skills
> provides services and support in bioinformatics and bioinformatics infrastructure through a dedicated bioinformatics facility

CMRI Bioinformatics will also play a key role in developing and establishing bioinformatics capability within the Westmead Research Hub and is working 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 Cell Cultures (ECACC) at the Health Protection Agency, 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

Confidence in cell lines. Integrity in research.
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.

Currently, Biomedical Proteomics 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 has also been provided by the Cancer Institute NSW, and 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 several large-scale, long-term studies with publication of results expected in 2014. In addition, in partnership with AB SCIEX, several smaller research and development projects were initiated, and preliminary data was reported at local and international meetings throughout 2013. These early successes have not only justified continued collaboration but also opened a number of different opportunities for scaling up joint research efforts.

The Facility has established an ongoing series of seminars, workshops and other educational and training opportunities for staff and students. In June 2013, Biomedical Proteomics organised and hosted the inaugural Chemical Proteomics Symposium highlighting the diversity of research projects and showcasing the strengths of recent technological advancements in this area.

In 2013, CMRI undertook a major upgrade of all Proteomics resources, which will culminate in the re-housing of the facility in a large, custom-designed, modern, multi-functional space in the Institute’s Stage 1 building redevelopment, due to open in June 2014.
ACRF Centre for Kinomics™

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 realize 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.
CMRI is a founding member of the Kids Cancer Alliance (KCA). KCA is an exciting and visionary initiative that will accelerate improvements in the survival rates and quality of life of children diagnosed with cancer in New South Wales and across Australia.

The Kids Cancer Alliance (KCA) brings together leading doctors and scientists working in child cancer medicine and research across NSW, to improve the care of children with cancer. KCA is an excellent example of ‘bedside-to-bench-to-bedside’ medicine, where the work of laboratory scientists is informed by clinical observations, and discoveries in the laboratory are translated into treatments that can be used in the clinic.

The Alliance came about as a result of a move in 2010 by the Cancer Institute New South Wales to establish four ‘Translational Cancer Research Centres’ state-wide. KCA is the only one of those centres solely focused on child cancer.

KCA encompasses the three child cancer-focused medical research institutes and the three clinical care centres in the state of NSW, in partnership with two major universities which support their research efforts – the University of NSW and the University of Sydney.

Member medical research institutes include Children’s Medical Research Institute, Children’s Cancer Institute, and the Kids Research Institute. The participating child cancer care centres are Sydney Children’s Hospital and The Children’s Hospital at Westmead (which together make up the Sydney Children’s Hospitals Network, SCHN), and John Hunter Children’s Hospital in Newcastle. Together, these hospitals treat more than 40% of Australia’s 600 newly diagnosed child cancer patients each year.

KCA’s vision is to bring doctors and scientists closer together to accelerate discovery and its application to improve the care of, and outcomes for, children with cancer.

All of the telomere researchers within KCA recently teamed up to form the ACRF Telomere Analysis Centre. The overall aim of this new research program is to understand the differences in telomere biology between normal and cancer cells in sufficient detail to be able to develop new cancer diagnostics, and most importantly to design novel broad-spectrum anticancer drugs that can potentially be used in combination with other treatments for almost all types of cancer. A lesser, but important, aim will be to understand the contribution of inter-individual variation in telomere biology to cancer predisposition.

**Kids Cancer Alliance Telomere Research Leaders**

1. Professor Roger Reddel MBBS BSc (Med) PhD FRACP FAA Lorimer Dods Professor and Director; Head, Cancer Research Unit (CMRI)

2. Associate Professor Tracy Bryan BSc (Hons) PhD Head, Cell Biology Unit (CMRI)

3. Dr Karen MacKenzie BASc PhD Leader, Cancer Cell Development Group (CCIA); Chair, KCA Telomere Research

4. Dr Hilda Pickett BSc(Hons) PhD Leader, Telomere Length Control Group (CMRI)

5. Dr Tony Cesare BSc PhD Leader, Telomeres and DNA Damage Group (CMRI)

6. Dr Loretta Lau MBBS (Hons) MMed PhD FRACP Leader, Neuroblastoma Research Group (SCHN)

7. Dr Julie Curtin MBBS PhD FRACP FRCPA Head, Department of Haematology (SCHN)

**Abbreviations:**

CCI  Children’s Cancer Institute  
CMRI  Children’s Medical Research Institute  
KCA  Kids Cancer Alliance  
SCHN  Sydney Children’s Hospitals Network.
Fundraising

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 sources, including the Jeans for Genes® campaign, community fundraising, bequests, direct marketing and a long-established investment fund.

The following pages highlight the achievements of CMRI’s fundraising programs in 2013 and acknowledge supporters who gave generously of their time and money to help create a healthier, brighter future for all children.
**Jeans for Genes** is one of Australia’s most recognised and loved charity campaigns and is the major fundraiser for Children’s Medical Research Institute.

*Jeans for Genes* celebrated its 20th anniversary supporting Children’s Medical Research Institute (CMRI) in 2013 with vigour, grace, enthusiasm, and a bigger street and online presence than ever before.

We had volunteers selling merchandise and collecting donations at 70 locations nationwide, with great performances by the Village Performing Arts Group, *Jeans for Genes* ambassador Adam Katz, and Prinnie Stevens from ‘The Voice’ at our flagship location in Martin Place, Sydney.

The campaign received more news coverage in states other than New South Wales than 2012 and supporter engagement online through social media sites, websites, and discussion forums was more vibrant than ever before.

We’ve received a number of emails from supporters across Australia sharing pictures, videos, and stories from the day, which shows how much they care about *Jeans for Genes* and want to help research at CMRI.

There was also great support shown by our corporate and retail partners; HCF, Big W, Lowes, Westpac, Gloria Jean’s Coffees, Glue Store, Calvin Klein Jeans, Outback Steakhouse, Sam’s Warehouse, Newcastle Permanent, Best & Less, P & N Bank, Crazy Clark’s, and Wide Bay Australia.

A big thank you also to our partners Toll, Direct Couriers, Sizzler, Technology One, G-Star Raw and Chubb, with support shown in many forms. Teams wore their jeans, decorated their offices and helped us raise much-needed funds by offering discounts to encourage supporter donations.

The campaign re-invents itself each year to maintain support, reach new audiences, and deliver a very important message – help us support Children’s Medical Research Institute by wearing your jeans and giving generously – in a fresh way.

It’s not every year you turn 20 and *Jeans for Genes* turned 20 with a bang.

Thank you to everyone involved, we’re very excited about the possibilities, ideas and involvement ahead to help us celebrate another major milestone in 2014 – the big two-one.
Jeans for Genes® Campaign
From the lion and zebra heads to the leopard print hats and pants – it is hard to pick just one standout moment at this year’s Jeans for Genes Gala Dinner.

The animal prints and costume store pick-ups meshed seamlessly with the bow-ties and ball gowns and, while the jeans for Genes team worked extremely hard to set the room alight with a touch of Africa, it was our guests who brought it to life.

Whether they were at the event or involved in our online auction – the atmosphere was electric.

We were able to raise $220,000 for Children’s Medical Research Institute, surpassing last year’s total.

A signed pair of singer/song-writer Seal’s jeans, transformed by artist Nafisa, sold for a whopping $18,000 on the night. The Bee Gees’ jeans were next on the top-selling list, followed closely by Ricky Martin’s. Both pairs were transformed into memorable artworks by Kathrin Longhurst and Garry Fleming, respectively.

Our MC, journalist and television personality Chris Bath, kicked off proceedings and helped lift the atmosphere to new heights with humour and grace.

But one of the most memorable speeches of the night was the heart-felt and very personal story shared by long-time CMRI supporter Linda Penn. It was a wonderful tribute to the work our scientists do and one which won’t be forgotten.

Linda’s daughter was born premature with life-threatening organ problems, and without immediate microsurgery the baby’s chance of survival was minimal. Microsurgery was pioneered at Children’s Medical Research Institute and if Linda’s daughter had been born just years before, the surgery would not have been available.

Alex is now an 18-year-old, heading towards a career in science, and one of the standout moments of the evening was when she appeared on stage at the end of Linda’s speech.

Director of Children’s Medical Research Institute, Roger Reddel, and Senior Research Scientist, Scott Cohen, also highlighted some of our greatest achievements. But most importantly, they encouraged us to look into the future. Not just a year down the track, but five years and ten years, with more research, greater discoveries and more lives saved or improved.

As Professor Reddel so eloquently put it, “You can’t accuse us of dreaming small.”

Thanks to everyone involved in making our 20th Jeans for Genes Gala Dinner such a memorable night, including our major sponsors: South African Airways, Bench International, Burwood Press, Decorative Events, Sofitel, Dr David and Mrs Linda Penn, and Robert Oatley.

A special thank you also to our volunteer Gala Dinner Event Committee Members, Patsy Cadell, Glenn A Baker, John Glover, Rod Glover, Patti Payne and Chris Lascaris.
The Great Cycle Challenge™ is a brand new fundraising initiative launched in 2013. Riders all across Australia took on a personal cycling challenge to pedal throughout October and fight kids’ cancer. Participants logged their kilometres via a GPS enabled app and used online fundraising pages to seek sponsorship. More than 2,650 riders participated, collectively raising more than $1.2 million for CMRI.

Many of the riders had a personal experience with children’s cancer. One such rider was Chris Hart, whose 6 year-old son, Ryan, was undergoing chemotherapy for leukaemia at the time. When Ryan heard his parents speaking about the Great Cycle Challenge, he was excited to get on his bike and be involved. The Harts decided to ride as a family and give back to the medical research that saved their little boy’s life.

Ryan was diagnosed just after his third birthday and was immediately put on monthly intravenous (IV) treatment and daily chemotherapy tablets. Throughout the treatments, Ryan’s parents were amazed by his capacity to remain cheerful and active. “We’d come out of an IV chemo treatment and drive past a tennis court and Ryan would beg to go in and play. Part of me wanted him to be resting on the couch, but I also wanted his life to be as normal as possible, and sport played a huge role in that for Ryan. He just loves being active - he’s really just a normal kid who has had to deal with a lot more than any child should ever have to.”

In October, Ryan had his last IV chemo treatment and was declared cancer free. In a letter to the participants in the challenge, Chris wrote: “For me, joining you in this event has been a great way to celebrate his cure and give back a little for all the support we have received over the last few years. I can absolutely tell you that what we have just been a part of will make a difference and save some children’s lives in the future. If it wasn’t for likeminded people raising money for children’s cancer research, we are today.”

The Great Cycle Challenge will be held again in October 2014. Participants wanting to be involved can visit greatcyclechallenge.com.au to find out more information and register. All funds raised from the challenge go towards fighting kids’ cancer through the ground-breaking research at Children’s Medical Research Institute.

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. 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. A list of their fundraising achievements can be found in the online addendum to this report. Some highlights from 2013, were:

- Vaucluse Committee Bill Waugh Memorial Cup Tennis Day
- Canberra Committee’s Annual Luncheon
- Hills Committee’s Mothers’ Luncheon
- Hills Committee’s Race Day
- Strathfield Committee’s June Gala Dinner
- Wagga Wagga Committee’s Christmas Fair
- Gerringong Committee’s High Tea
- Gerringong’s Famous Annual Quilt Show
- Gosford Committee’s Christmas Garden Party
- Port Hacking Luncheon, 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, Northern Beaches Committees
- Quiz Night – Strathfield, Gosford Committees
- Discovery Day catering – Beecroft Committee
- Maroota Fashion Shows
- Kuring-gai Film Night

Other wonderful community supporters include: Trivett Class BMW Parramatta, with 11 years of support for the Golf Day; Rotary Club of Cessnock Wine Country; and Treasury of Craft, with 21 years of dedicated fundraising via craft stalls.
Major Supporters and 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, Mrs Joan M Barnet, Beryl Raymer, Joan Mackisack, Ann Jolly, Kenneth Reid, Wendy Tonkin, Woolworths Support Office Bella Vista, Franklins, and J.J. Richards & Sons.

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, and the Sir Norman Gregg Fellowship.

Our corporate partners are important to our fundraising efforts, and we are fortunate to have long standing relationships with a number of companies. Star Alliance initially joined us in 2010 and has since been actively fundraising through ticket sales and other means to support CMRI, as well as providing travel scholarships for CMRI PhD students.

Some of our corporate supporters provide a combination of pro bono services and financial sponsorship. Particular thanks goes to Westpac, Technology One, Addisons Lawyers, Allens<->Linklaters, and AB Sciex for their generous support throughout 2013, as well as to YuHu Group for their significant $1 million contribution to our capital building project.

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.

Bequests

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. If you would like more information on leaving a bequest in your will please contact bequests@cmri.org.au or call 1 800 436 437.

A Message from Star Alliance

We launched the Star Alliance Scholarship in 2010 as part of our association with the Children’s Medical Research Institute - an independent Australian organisation conducting genetic research to help prevent and treat childhood diseases.

The aim of the annual award was to enable a PhD student to travel on a Star Alliance Round the World airfare to international conferences or events that would help them build their knowledge and professional networks, and hopefully assist them to land a post-doctoral position.

Here is a quick update on where our previous winners are now and how the Scholarship has helped them move forward with their careers.

The inaugural winner of the Star Alliance Scholarship was Josh Stern, who used his ticket to attend an international conference in France in October 2010, where he presented his research on an enzyme called telomerase, which is involved in up to 90% of all types of cancer. Josh is now a postdoctoral fellow in the laboratory of Nobel Laureate, Professor Tom Cech, in Colorado, and his PhD supervisor at CMRI, Associate Professor Tracy Bryan, says the fact that he had presented his work at an international conference undoubtedly helped him obtain a position in the US.

Our 2011 winner Allison Dane used the Scholarship to attend a conference on gene therapy in Brighton, England in October 2011, and to visit a number of labs throughout the UK and Europe.

As a direct result of the trip, Allison subsequently secured a position in the Research Department of Haematology, at University College, London, where she is now based.

The 2012 Scholarship winner Claire Deakin travelled with Star Alliance members to a meeting of the American Society of Gene and Cell Therapy in Philadelphia, then on to the UK where she also visited leading research laboratories. Once again the connections forged during the trip resulted in Claire also being offered a research position in London. And in fact, I’m pleased to say that she is now working – almost alongside – Alison at University College, in the Institute of Child Health.

The 2013 winner was Lia Moshkanbaryans. Lia is a PhD student in Neuroscience/Biochemistry in the CMRI’s Cell Signalling Unit, and she used the Scholarship to travel to Vienna to attend BIO-Europe 2013 – a major gathering of European and US scientists interested in the fast-growing field of science commercialisation.
## Media Report

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**Overall CMRI media news stories Jan-Dec 2013**

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CMRI has initiated plans for a redevelopment on our existing site to provide us with the space and requirements needed to maximise our research potential and take our discoveries to the next level for the benefit of children and their families.

Our current building is at capacity and needs to expand in order to support our expanding research efforts, accommodate greater student intake, to provide improved infrastructure for specialised technologies, and to allow space for our growing national facilities. In addition, many of our core research programs are reaching developmental stages that will greatly benefit from greater depth and breadth of research and support staff, leading to better and faster translation into health outcomes for children and financial returns which will support further research.

To achieve this expansion of our research efforts, CMRI has plans to redevelop its building from its current two storeys to seven storeys in five stages (with planning approvals already received). It is to be completed with minimal disturbance to current research activities, where the new stages integrate seamlessly with the existing structures.

The first completed stage of the building plans will officially open in August 2014.

This Stage 1 building will increase our capacity by two thirds and provide space for several of our key research facilities: The ACRF Centre for Kinomics, The ACRF Telomere Analysis Centre, and Bioinformatics.

We are seeking additional funds from private and government sources to complete the internal fit-out of some laboratory spaces and research floors. CMRI's
Capital Foundation is dedicated to finding the necessary support for the full costs of Stage 1 as well as funds for additional stages. The second stage will commence when a further $55m of funding is committed.

**Westmead Research Hub**

CMRI’s proposed redevelopment is part of ongoing development plans for the whole Westmead precinct which will create a world-leading centre for health care and medical research and become the largest such precinct in Australia.

The Westmead Research Hub is a coalition that includes CMRI, Westmead Hospital (WH), Children’s Hospital Westmead (CHW), Westmead Millennium Institute (WMI), and The University of Sydney (USYD). Scientists across the Hub collaborate, sharing knowledge and expertise. The Hub also coordinates the purchase and sharing of major, high-tech equipment and other core technologies; and seeks to create education and training pathways for students and young researchers.

All of the research programs at CMRI and in the Westmead Research Hub benefit from the shared resources, such as Advanced Microscopy and Imaging facilities (including an Electron Microscope Laboratory), CMRI’s own Biomedical Proteomics Facility, advanced Flow Cytometry and Analysis systems and the Sydney Cell and Gene Therapy laboratories.

CMRI is a founding member of the Westmead Research Hub and a strong advocate for its continued growth, helping to make Westmead and Western Sydney the site for major Australian research efforts and a major source of economic and technical skills growth in this important sector.
CMRI is an independent research institute based in Westmead, NSW. The Institute employs approximately 170 people, including 110 full-time scientists and PhD students, as well as operational and administrative support staff and a small 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.
Board of Directors

CMRI is managed by a Board of Directors, consisting of thirteen independent, non-executive directors and one executive director. Board members bring a wide range of business, commercial and scientific expertise to CMRI.

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.

Directors in Office are:

Professor Frank Martin (MBBS FRANZCO FRACS AM Oph), President

Frank Martin is a visiting ophthalmologist at The Sydney Children's Hospitals Network at Westmead and Randwick and at Sydney Eye Hospital. He is past President of the Asia-Pacific Academy of Ophthalmology and President of the Asia-Pacific Society of Paediatric Ophthalmology and Strabismus and the International Strabismus Association.

He serves on the Board of Trustees of the American Academy of Ophthalmology and the International Council of Ophthalmology (ICO) and has recently been appointed Director of Society Development and Leadership for the ICO. He is the Vice Chairman of RANZCO Foundation and was President of the Royal Australian and New Zealand College of Ophthalmologists from 1996 to 1997.

He is also Chairman of the Westmead Research Hub and on the Board of the Lowy Medical Foundation. Professor Martin has been a CMRI Board member since 1986 and was elected President in April 2000.

Professor Martin serves on the Institute’s Audit and Risk Committee, Finance and Investment Committee, Intellectual Property Committee and chairs the Nominations and Remuneration Committee. He is also an Executive Member of the CMRI Capital Foundation.

Mrs Carolyn Forster (OAM), Vice President

Carolyn Forster has been a member of the Canberra Committee of CMRI since 1973, serving three times as President and twice as Treasurer. She worked in the Federal Parliament for 11 years, in the Senate, the House of Representatives, and the Ministry.

She chaired the ACT Heritage Festival for 11 years, chaired the Board of Phillip College and was a Past President of the Women’s International Club, ACT. Mrs Forster is currently a committee member and a former President of the Friends of the National Museum of Australia. She is also the former Vice-President of the World Federation of Friends of Museums (WFFM) for Africa, Asia, Pacific. She is currently the Australian Delegate to the WFFM, a member of the Australian Executive Committee of the International Council of Museums (ICOM), a committee member of the Australiana Fund and Chair of the Church of St Andrew Conservation and Restoration Foundation.

She received an ACT Women’s Award in 1996, a Centenary Medal in 2003, and an OAM in 2006. Mrs Forster joined the Board in 1996 and was elected Vice-President in 2000. Mrs Forster serves on the Institute’s Finance and Investment Committee, Audit & Risk Committee, and Nominations & Remuneration Committee. Mrs Forster also chairs the Capital Foundation.

Mr Rodney Atfield (FIA FIAA FAII), Treasurer

Rodney Atfield was formerly the Managing Director of the Mercantile Mutual (now ING) group of companies and was Chairman of QBE Mercantile Mutual Limited. He is an actuary by profession and is a former President of the Institute of Actuaries of Australia and is a Life Member of that Institute. He has been a director of a number of public companies, APRA, a number of industry bodies and was Chairman of Macquarie University Actuarial Foundation. He has been involved in several task forces and advisory bodies to federal government. Currently, he is a director of Hannover Life Re and ING Bank Foundation. Mr Atfield’s extensive experience in actuarial management and financial administration led to his appointment to the Board of CMRI in February 2001 and election as Treasurer in December 2001. Mr Atfield chairs the Institute’s Audit and Risk Committee and Finance and Investment Committee. He is also a member of the Intellectual Property Committee and the Nominations and Remuneration Committee.

Professor Ian Caterson (AM MBBS BSc(Med) PhD FRACP)

Ian Caterson is Boden Professor of Human Nutrition and Foundation Director of the Boden Institute of Obesity Nutrition Exercise & Eating Disorders, University of Sydney. Previously, he was Senior Staff Specialist and Director of Clinical Endocrinology at Royal Prince Alfred Hospital. He was a post-doctoral researcher at the University of Oxford with Professor Sir Philip Randle FRS.
His research interests have been in insulin resistance and the causes, prevention and treatment of obesity and the prevention of chronic disease. He is a past president of the Australian Diabetes Society and the Australasian Society for the Study of Obesity. He was previously Head of the School of Molecular & Microbial Biosciences at the University of Sydney. He has been a regional advisor on obesity for the World Health Organisation (WHO) and to Australian governments. He is Past President (Asia-Oceania) for the International Association for the Study of Obesity (now World Obesity). He is President-elect of World Obesity.

Professor Caterson joined the Board of CMRI in 2004 and is a member of the Institute’s Intellectual Property Committee.

The Hon Craig Knowles
Craig Knowles holds a number of advisory roles and directorships in the health, finance, property, planning and aged care sectors. His roles include President, Planning Research Centre, Faculty of Architecture, Planning and Design, Sydney University; Trustee of the Hoc Mai Foundation; Director, Black Dog Institute; Non-Executive Director, SW Sydney Medicare Local Transition Board; Member, Central Sydney Planning Committee; Advisor, Investec Bank (Australia) Ltd; Director, Tulich Family Communities Aged Care; Independent Chairman, Prospect Water Partnership; and Member, Built Holdings Advisory Board.

Mr Knowles was a senior Minister in the New South Wales Government for 10 years serving in the portfolios of Planning and Housing (1995–99), Health (1999–2003), Infrastructure, Planning and Natural Resources (2003–August 2005); Minister for Forests and Minister for Lands (2003–January 2005) and immediate past President, Asthma Foundation, NSW. On 28 January 2011, Mr Knowles was appointed as the Chairperson of the Events and Hospitality Committee of the Clancey Donald Foundation and on the governing council of the Global Health Institute. His research group focuses on the genetics of autoimmune disease, particularly multiple sclerosis, HIV and allergies. He is a past Chairman of the Westmead Medical Staff Council and is co-chair of the NSW Medical Staff Executive Council. He has also been deputy chair of the Greater Metropolitan Clinical Taskforce. He has served on the CMRI Board since 2002 and is Chair of the Institute’s Intellectual Property Committee.

Professor Roger Reddel (BSc (Med) MBBS PhD FRACP), CMRI Director
Roger Reddel heads CMRI’s Cancer Research Unit and is the CMRI Director and Lorimer Dods Professor, Sydney Medical School, University of Sydney. He obtained medical degrees from the University of Sydney and trained in medical oncology at the Royal Prince Alfred Hospital. Professor Reddel completed a PhD in cancer cell biology at the Ludwig Institute for Cancer Research, University of Sydney, and received an NHMRC CJ Martin Fellowship and a Fulbright Fellowship to undertake postdoctoral research at the National Cancer Institute, Bethesda, Maryland. He returned to Sydney to establish a laboratory with the support of Cancer Council NSW’s Bicentennial Fellowship. In 2007, Professor Reddel was awarded the Ramaciotti Medal for Excellence in Biomedical Research, in 2010 was elected as 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

Mrs Patricia Payne (OAM MPS PhC)
Patti Payne has been a Community Pharmacist for over 25 years, practising on the Central Coast, NSW. She joined the Beecroft Committee of CMRI in 1969, serving as President from 1972 to 1973. In 1991, she was instrumental in forming the Hills Committee and has been its President ever since. She is a member of CMRI/CHW Institutional Biosafety Committee and has been heavily involved with Jeans for Genes since its inception. She has served on the Board of Trustees of the Kings School Foundation and has organised many functions for other institutions and charities. She is the foundation President of the Women for Pharmacy network, Chairperson of the Events and Hospitality Committee of the Federation Internationale Pharmaceutique (FIP) World Conference, Sydney, 2003 and is the Australian nominee to the Board of Directors of the Community Pharmacy Section of FIP. She has four adult children and the fifth died in infancy from a genetically related condition. She was awarded the Medal of the Order of Australia in 2006. Ms Payne was elected to the Board in October 2000.

Clinical Professor Graeme Stewart (AM BSc(Med) MBBS PhD FRACP FRCPA)
Graeme Stewart was appointed as founding head of Immunology at Westmead Hospital in 1980. He is the Inaugural Director of the Institute for Immunology and Allergy Research, one of the four founding research groups of the Westmead Millennium Institute. Professor Stewart was the Inaugural President of the Australasian Society for HIV Medicine and has played a role at a national and international level in HIV policy, medical education and research. He is a member of the board of Multiple Sclerosis Research Australia, Chair of the Clancey Donald Foundation and on the governing council of the Global Health Institute. His research group focuses on the genetics of autoimmune disease, particularly multiple sclerosis, HIV and allergies. He is a past Chairman of the Westmead Medical Staff Council and is co-chair of the NSW Medical Staff Executive Council. He has also been deputy chair of the Greater Metropolitan Clinical Taskforce. He has served on the CMRI Board since 2002 and is Chair of the Institute’s Intellectual Property Committee.
is an editorial board member of several cancer journals, serves on national and international advisory boards, and is a Director of Cure Cancer Australia Foundation. Professor Reddel has been Director of the Institute since 2007 and serves on the Institute’s Finance and Investment Committee.

Mr Albert Wong
Originally from Hong Kong, Mr Wong has lived in Australia for over 37 years and has been involved in the stockbroking and investment banking industry for over 30 years. He was admitted as a Member of the Australian Stock Exchange in 1988 and was the principal of Intersuisse Limited until 1995 when he established the Barton Capital group of companies, including eStar, both companies listed on the Australian Securities Exchange. He was the business partner of former NSW Premier, The Hon. Neville Wran AC QC at Wran Partners from 2004 – 2011.

Currently, Mr Wong is Chairman of Winmar Resources Limited and Deputy Chairman of Prima BioMed Limited and Kimberley Diamonds Limited. Mr Wong has been widely involved in philanthropic activities including his directorships on UNSW Foundation, Ian Thorpe’s Fountain for Youth Foundation and Honorary Life Governor and President of the Physics Foundation at the University of Sydney. Mr Wong is a Fellow of the Financial Services Institute of Australia and a Fellow of the Australian Institute of Company Directors. Mr Wong joined the CMRI Board in October 2013. He is also an Executive Member of the CMRI Capital Foundation.

Mr Bruce Fink
Bruce Fink achieved a Business Degree majoring in banking and finance at Melbourne’s Monash University. His 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. Mr Fink conducts philanthropic activities, particularly in relation to education and health, both in Australia and abroad. These include the Lauren and Bruce Fink School of Information Technology at Mt Scopus College in Victoria; the Leon Fink Middle School at Moriah College in Sydney; and the new Lauren & Bruce Fink Paediatric Emergency Theatre at Sydney Children’s Hospital in Randwick, New South Wales. Mr Fink also serves on the Board of the Moriah College Foundation.

Mr Fink joined the CMRI Board in August 2013. He serves on the Institute’s Finance and Investment Committee and the Audit & Risk Committee. He is also an Executive Member of the CMRI Capital Foundation.

Dr Luciano Dalla-Pozza *(MBBS FRACP)*
Luciano 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 including the Australian and New Zealand Children’s Cancer Study Group, the Australasian Leukaemia and Lymphoma Group, the Children’s Oncology Group (USA), and the Clinical Oncological Society of Australia. His interest and work has centred on the management of acute leukaemia in children and adolescents, the development of clinical trials in paediatric oncology and the development of basic research opportunities. He is the Study Chairperson of the ANZCHOG Acute lymphoblastic Leukaemia Study 8 Clinical trial and Co-chair of the Leukaemia-Lymphoma Committee of the Australian and New Zealand Children’s Haematology-Oncology Group.

Dr Dalla-Pozza joined the CMRI Board in September 2013.

Mr Michael Loughman
Michael Loughman is employed by Australia & New Zealand Banking Group Limited where he 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 & Wealth Management professional with a career spanning 18 years both domestically and globally. Prior to ANZ Bank, Mr Loughman worked for Deutsche Bank Private Wealth Management & Royal Bank of Scotland. Mr Loughman joined the CMRI Board in August 2013. He serves on the Institute’s Finance & Investment Committee and the Audit & Risk Committee.

Ms Fiona Crosbie *(BA LLM)*
Fiona 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 a member of the Competition and Consumer Committee of the Law Council of Australia and of the Advisory Board to the University of Melbourne for postgraduate competition law studies. Her work includes advising in the pharmaceutical and medical device industry sectors in relation to a range of legal and regulatory issues. Ms Crosbie joined the CMRI Board in August 2013 and serves on the Institute’s Audit & Risk Committee.
Insight: John Dunlop

“The more you learn (about CMRI), the more you realise you don’t know. It’s worth fighting for and worth trying to encourage others to do the same.”

More than 43 years ago, former CMRI board member, John Dunlop, was inspired to join the team by Sir Lorimer Dods.

“I stress, I wasn’t a scientist or researcher,” John said, “but I believed in why CMRI was founded, and I believed that was worth fighting for.

“Our (the Board’s) job was to foster the ideas that were given birth by Lorimer Dods, which was to provide the means and the place where scientists and researchers of good calibre would want to join and search for causes and cures of childhood diseases.

“Lorimer was a very inspirational man.”

John helped develop CMRI from modest beginnings to the world-leading centre of medical research it is today.

Despite his achievements in helping develop the dream fostered by Sir Lorimer, John’s modesty hasn’t wavered.

“I played my part, but it was a team effort.”

A team which John decided it was time to leave in October 2013. His reasons just as admirable as those for which he joined.

“Why am I going now?” he said. “Age – it’s somebody else’s turn, and it’s exactly why I was brought in 43 years ago. I was basically there to bring business thinking, experience, and sense to protect and try to attract and help build up CMRI’s resources. To help turn an idea into reality – to help inspire.

“The more you learn (about CMRI), the more you realise you don’t know. It’s worth fighting for and worth trying to encourage others to do the same.

“It’s time for me to give someone else the opportunity I had 43 years ago.”

John has not lost an ounce of passion or respect for the cause he has been part of for so long, which is tribute not only to John as a person, but also to the kind of people CMRI attracts... and holds on to. John has resigned from the Board but has now joined CMRI’s Nominations and Remuneration Committee.

Thanks to people like John, Sir Lorimer Dods’ dream is looking brighter than ever.
Committees and Advisory Boards

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:
> Prof. Frank Martin
> Mrs Carolyn Forster
> Mr Rod Atfield (Chair)
> Mr Bruce Fink
> Mr Michael Loughman
> Ms Fiona Crosbie

Finance & Investment Committee
The Finance and Investment Committee manages and monitors the performance of CMRI’s investment portfolio. Committee members include:
> Prof. Frank Martin
> Mrs Carolyn Forster
> Mr Rod Atfield (Chair)
> Prof. Roger Reddel
> Mr Ralph Mitchell
> Mr Bruce Fink
> Mr Michael Loughman
> Mr Paul Scully
> Dr Don Stammer

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
> Mr John Dunlop

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
> Prof. Frank Martin
> Mr Rod Atfield
> Mr Ralph Mitchell
The Organisation

CMRI Board of Directors

Intellectual Property Committee
Audit & Risk Committee
Director
Capital Foundation
Finance & Investment Committee
Nominations & Remuneration Committee

Operations

Lab Management
Bio Resources
Building Facilities
Information & Communications Technology

Research

Cancer Research
Cell Biology
Cell Cycle
Embryology
Gene Therapy
Cell Signalling
Protein Biochemistry
Eye Genetics
Genome Integrity
Telomere Length Regulation

Specialised Facilities

CellBank Australia™
Bioinformatics
Biomedical Proteomics Facility (including ACRF Centre for Kinomics™)
ACRF Telomere Analysis Centre

Executive

Director’s Office
Finance and Grants Management
Human Resources
Commercialisation & Affiliations
Marketing & Communications
Supporter Services
Building Redevelopment Project

Fundraising

Jeans for Genes®
Community Fundraising
Philanthropy & Major Partnerships
Bequests
Capital Campaign

Management and Operations Committees

Animal Care & Ethics
Work Health & Safety
Institutional Biosafety
Scholarships
Grants Advisory
Appointments
Promotions

Advisory Committees

Scientific Advisory Centre for Kinomics™
Scientific Advisory CellBank Australia™
Cancer Consumer Panel
CMRI’s finances continue to be sound and it is pleasing to report the continuation of good performance across the board again this year. This has allowed us to spend over three quarters of every dollar of total revenue on our research again this year. In addition, our balance sheet is bolstered by strong investment revaluations and recognition of capital grant income related to our building redevelopment.

At 31 December, 2013, our total assets have grown to just over $121.5 million with our equity (or net assets) representing $106.9 million of that figure. Comprehensive income for the year was $19.8 million (2012 - $4.9 million), including capital grant income for our building of $12.4 million (2012 - $2 million).

Although our operating revenue did not increase over 2012, it is important to note that our revenues exclude the significant rises in investment valuations throughout the year and the profits realised on investment sales. Both these items appear separately in the Statement of Comprehensive Income. Our total investment returns for the year were 15%, derived from an investment portfolio comprising both growth and defensive assets. This return was significantly higher than our investment target and was attributable to stronger equity markets around the world than we have seen in the years since the 2007-08 global financial crisis.

Our researchers continued to demonstrate the high quality of our research, successfully being awarded new funds and commencing several new projects based on competitively won grants. Research grant income is just over $7 million of our Total Revenue. Building redevelopment aside, our capital grants income for equipment was lower in 2013, after a major grant of $3 million was earned in 2012 million from the Australian Cancer Research Foundation (ACRF), and used to establish the ACRF Centre for Kinomics. In 2013, CMRI has been awarded another of these prestigious grants, for $2 million, which will be earned in 2014 when we establish the ACRF Australian Telomere Analysis Centre in our new building space. Both of these facilities will be significant contributors to Australia’s cancer research in the years to come.

Our regular fundraising income was significantly higher in 2013 at $11.7 million (2012 - $6.6 million) with only a $0.7 million rise in related costs. A number of factors contributed to this change. Jeans for Genes® continues to be one of the most recognisable charity brands in Australia and every year generates a significant revenue stream for us in an increasingly crowded market place. In 2013, we held the inaugural Great Cycle Challenge™, which became the best performed first-year digital fundraising event in the nation, generating over $1 million of revenue. We also received several major bequests in our name during 2013. Separately, we also received $1.1 million in philanthropic donations towards our Capital Campaign for our building redevelopment program.

Our strategy moving forward will continue to be one of looking to grow our revenue streams with manageable risk, while controlling costs. We are due to complete the first stage of our building redevelopment in June of 2014, representing the first step in a strategy for the Institute to develop and grow its research base. Not only will we be introducing new, specialised facilities and expanding on current ones such as those mentioned above, but we plan on recruiting new scientific leaders in our core research areas, commencing in 2015. It is therefore important that we continue to invest in revenue growth strategies so we can fund further development, and pleasing to do so without diminishing overall financial performance. We look forward to continued success in 2014.
Sources of Income\(^1\)

<table>
<thead>
<tr>
<th>Sources of Income</th>
<th>YTD December 2013</th>
<th>YTD December 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>$31 million</td>
<td>$27 million</td>
</tr>
</tbody>
</table>

- Grants for Research: 26%
- Fundraising: 39%
- Investment Return*: 35%
- Grants for Research: 41%
- Fundraising: 26%
- Investment Return*: 33%

\(^1\) Income excludes Building Redevelopment Grants/Donations but includes Total Investment Return.

* Total Investment Return includes dividend distribution, profit/loss on redemption and comprehensive income on available-for-sale financial assets.

Sources of Expenditure

<table>
<thead>
<tr>
<th>Sources of Expenditure</th>
<th>YTD December 2013</th>
<th>YTD December 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>$24 million</td>
<td>$24 million</td>
</tr>
</tbody>
</table>

- Research: 75%
- Fundraising: 16%
- Corporate Administration: 9%
- Fundraising: 13%
- Corporate Administration: 8%
- Research: 79%
Sources of Revenue

<table>
<thead>
<tr>
<th></th>
<th>YTD December 2013</th>
<th>YTD December 2012</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td>$36 million</td>
<td>$25 million</td>
</tr>
<tr>
<td>Fundraising</td>
<td>33%</td>
<td>27%</td>
</tr>
<tr>
<td>Building Redevelopment</td>
<td>38%</td>
<td>8%</td>
</tr>
<tr>
<td>Grants for Research</td>
<td>22%</td>
<td>44%</td>
</tr>
<tr>
<td>Investments</td>
<td>7%</td>
<td>21%</td>
</tr>
</tbody>
</table>

2 As per Audited Accounts year ended 31 December

Statement of Assets (at 31 December)

<table>
<thead>
<tr>
<th></th>
<th>2013</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td>$122 million</td>
<td>$111 million</td>
</tr>
<tr>
<td>Financial Assets</td>
<td>56%</td>
<td>48%</td>
</tr>
<tr>
<td>Property, Plant and Equipment; other non current assets</td>
<td>26%</td>
<td>18%</td>
</tr>
<tr>
<td>Cash, restricted for Building Redevelopment</td>
<td>9%</td>
<td>17%</td>
</tr>
<tr>
<td>Current Assets, excluding Restricted Cash</td>
<td>9%</td>
<td>17%</td>
</tr>
</tbody>
</table>
# Financial Summary

## Profit and Loss Statement

<table>
<thead>
<tr>
<th></th>
<th>YTD Dec 2013 (in $ '000s)</th>
<th>YTD Dec 2012 (in $ '000s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revenues</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research</td>
<td>7,983</td>
<td>10,808</td>
</tr>
<tr>
<td>Fundraising</td>
<td>11,822</td>
<td>6,801</td>
</tr>
<tr>
<td>Investments</td>
<td>2,624</td>
<td>5,336</td>
</tr>
<tr>
<td>Building redevelopment</td>
<td>13,532</td>
<td>1,986</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>35,961</td>
<td>24,931</td>
</tr>
<tr>
<td><strong>Expenses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research</td>
<td>18,248</td>
<td>18,523</td>
</tr>
<tr>
<td>Fundraising</td>
<td>3,818</td>
<td>3,125</td>
</tr>
<tr>
<td>Administration and facilities</td>
<td>2,244</td>
<td>2,007</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>24,310</td>
<td>23,655</td>
</tr>
<tr>
<td><strong>Surplus/(loss) before investment transactions</strong></td>
<td>11,651</td>
<td>1,276</td>
</tr>
<tr>
<td>Investment transactions, net</td>
<td>1,049</td>
<td>1,131</td>
</tr>
<tr>
<td><strong>Surplus/(loss) from continuing operations</strong></td>
<td>12,699</td>
<td>2,406</td>
</tr>
<tr>
<td>Other comprehensive income from available-for-sale financial assets</td>
<td>7,106</td>
<td>2,526</td>
</tr>
<tr>
<td><strong>Total comprehensive income/(loss) for the period</strong></td>
<td>19,805</td>
<td>4,933</td>
</tr>
</tbody>
</table>

## Balance Sheet

<table>
<thead>
<tr>
<th></th>
<th>As at: 31 Dec 2013 (in $ ’000s)</th>
<th>As at: 31 Dec 2012 (in $ ’000s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current assets, including cash &amp; term deposits*</td>
<td>21,839</td>
<td>37,034</td>
</tr>
<tr>
<td>Other financial assets</td>
<td>68,420</td>
<td>54,086</td>
</tr>
<tr>
<td>Property, plant and equipment</td>
<td>30,454</td>
<td>18,408</td>
</tr>
<tr>
<td>Other non-current assets</td>
<td>808</td>
<td>1,238</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>121,521</td>
<td>110,766</td>
</tr>
<tr>
<td><strong>Liabilities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current liabilities**</td>
<td>14,393</td>
<td>23,477</td>
</tr>
<tr>
<td>Non-current liabilities</td>
<td>242</td>
<td>208</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>14,635</td>
<td>23,685</td>
</tr>
<tr>
<td><strong>Net Assets</strong></td>
<td>106,886</td>
<td>87,081</td>
</tr>
</tbody>
</table>

* Included in deposits is an amount of $10.6 million (2012: $18.7 million), which is restricted for use under the terms of the Building Redevelopment Capital Grant

** Included $7.0 million (2012: 18.8 million) of Deferred Income from Building Redevelopment Capital Grant of $20 million

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 www.cmri.org.au/About-Us/Annual-Reports-and-Financial-Statements
We thank 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.