Today’s scientists for tomorrow’s children
Welcome and Introduction

Welcome to our annual report outlining our work and achievements over the 18 month period from July 2009 through to December 2010. In 2010 CMRI moved its year end to December to better align accounting and reporting requirements with the timing of funds received by the Institute. Our next financial year end will be December 31, 2011 and then every 12 months thereafter.

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Report from the Director

"To speed up the pace of research, and to increase the rate at which discoveries in the laboratory are turned into new treatments, CMRI needs many more researchers and expanded research facilities."

Frank Reddel
Director
July 2011

2010 and the latter half of 2009 was a period of change for Children’s Medical Research Institute and I am pleased that we have effectively met all challenges that inevitably come with such change. Most of all, I am delighted to report that CMRI is now well positioned for future growth.

As you know, the global financial crisis continued to impact the economy well into 2010 and, as a charity, our revenues were understandably affected. While the last six months of 2010 showed an operating profit, we still face an economy where investment returns are uncertain, federal budget deficits continue to threaten medical research funding and natural disasters impact community fundraising.

Nevertheless, thanks to the work of our talented researchers, CMRI continues to advance the prevention and treatment of disease, which will give all children a chance at a healthier future. Each of our research areas – embryonic development and birth defects, cancer, cell signalling and gene therapy – has made great strides in the past 18 months.

Our 25 fundraising committees provide a vital link to the community. Through their devotion and energy they help spread the news on CMRI’s outstanding research efforts, and raise much needed funds. In this reporting period, our local community committee networks have raised close to $500,000 – an exceptional achievement.

Our income from research grants has remained strong through this last eighteen months generating approximately $16 million for the Institute’s bottom line. Fundraising efforts yielded $12 million with approximately half of this income achieved through the annual Jeans for Genes® national campaign.

I am also delighted to announce a raft of achievements in the area of governance. In particular, I congratulate the Board, its sub-committees and management on improving overall governance of CMRI. Our aim is to be the best in ‘research and corporate’ governance in the medical research and charity sectors. Included in our achievements is the introduction of a Nominations and Remuneration Committee, to manage the appointment of new Board members based on required expertise.

In addition, our Finance and Investment Committee has overseen the appointment of new members with specialised professional finance skills. In the wake of the global financial crisis, this Committee conducted a full review of our investment strategy and portfolio and I am pleased to report that our Investment Fund has regained its upward momentum.

Our Intellectual Property Committee has been busy thanks to major research advances. Several research programs have made discoveries that add to the Institute’s body of research and intellectual property. Through new and ongoing research collaborations, there is potential for these programs to be translated into major health outcomes and, ultimately, commercial returns. We hope that some of these opportunities will not only advance medical science, but deliver new income streams to the Institute in the future.

On behalf of the Board, I convey warm congratulations to Professor Roger Reddel who was elected Fellow of the Australian Academy of Science in 2010 for his outstanding scientific achievements in cell immortalisation and his lifelong contribution to science.

More recently, Professor Reddel received the Premier’s Award for Outstanding Cancer Researcher of the Year, and Professor Patrick Tam was elected as a Fellow of the Royal Society, which is one of the highest international honours for a scientist. More details about these awards will be provided in the 2011 Annual Report.

I would like to thank and acknowledge all of CMRI’s scientists and research students for their contribution to maintaining CMRI as a leader in research in Australia. I would also like to acknowledge management, administration and all the staff of the CMRI for their continued support and contribution.

Under Professor Reddel’s direction, the outlook for CMRI is positive. Lastly, as always, we are grateful to all our supporters and volunteers who give generously of their time, commitment and funds.

Frank Martin
President
July 2011

Thanks to the wonderful support we receive from the community, Children’s Medical Research Institute (CMRI) has continued to make excellent progress in all of its research areas. I can highlight only a few of the advances here, and more details are given in the pages describing the achievements of each of our research units.

During the period covered by this report, the work that attracted most attention was the discovery by Dr Jeremy Henson in the Cancer Research Unit of a very unusual form of DNA in a specific subset of cancers and in the blood of patients with these types of cancers. This discovery will improve cancer diagnosis, and will speed up the search for anticancer treatments for these cancers. The Cell Biology Unit has significantly advanced our understanding of the function of telomerase, an enzyme that is critically important for the continued proliferation of 85% of all cancers, and the Cell Transformation Unit made important discoveries about the p53 protein, which is probably the most important of all the proteins that protect us against cancer. The Embryology Unit made great progress analysing the congenital abnormalities in the face, fingers and forearms that are caused by deficiencies in a gene named Twist-1. A major discovery by the Cell Signalling Unit and overseas collaborators was that two proteins (GSK3 and cdk5) act in partnership to control the rate of nerve cell communication when the cells are highly stimulated, as occurs in epilepsy. This has implications for treating epilepsy, and a range of other neurological disorders.

The Gene Therapy Unit has made substantial progress towards being able to treat children born with life-threatening inherited liver disorders.

CMRI provides two important facilities for researchers throughout Australia. CellBank Australia supplies high-quality cell lines and cell line testing services that underpin many biomedical research activities. The Centre for Biomedical Proteomics is a unique, cutting-edge national facility that will facilitate development of drugs for a very wide range of medical conditions.

Welcome and Introduction
Cell Signalling Unit

Our research team focuses on understanding the normal signalling events inside cells that allow nerve cells to communicate. Surprisingly similar mechanisms also control the last stage of the cell division cycle. One way these are connected is called endocytosis — whereby cells internalise signals or nutrients from the outside. Understanding how this occurs and is controlled will help us develop means to control nerve communication, and hence control diseases such as epilepsy, or to stop the cell division cycle, hence preventing the growth of cancers like glioblastoma in the brain.

Many genes are required for endocytosis but the master regulator is dynamin. Of the three dynamin proteins in the body, we study dynamin I (dynl) and dynamin II (dynll). As we learn more, dynamin continues to surprise us with its multiple cellular functions and the complex mechanisms cells use to restrict its activity.

Highlights and Future Plans

We have developed a drug discovery program with Professor Adam McCluskey at the University of Newcastle. In collaboration with our research partners, we designed compounds that inhibit dynamin (dynamin inhibitors) and published three new classes which we call the dynoles, the iminochromenes and the pthaladyns. As expected, each of these compounds block endocytosis in cells, but we also demonstrated two additional uses. Firstly, they block the uptake of certain viruses into cells, suggesting they may be of future use to treat infectious diseases. Secondly, we showed that they block cell proliferation and cause cell death in human cancer cells. This exciting study demonstrates their potential to be developed into novel anti-cancer drugs in the long term. We look forward to being able to generate many new and more potent dynamin inhibitors, with the hope that we can distinguish between dynl and dynll activity to individually target compounds for epilepsy or glioblastoma treatments.

We have made several discoveries that improve our understanding of cell division. We showed that dynll is a master controller of the last few minutes of the cell cycle. In a series of landmark studies we reported a signalling cascade in cells that keeps dynll quiescent throughout the cell cycle by phosphorylation. Yet by engaging calcineurin, the cell can rapidly activate dynamin within seconds to complete the cell cycle and permit separation into two daughter cells (this stage is called cytokinesis). These discoveries explain why our dynamin inhibitors prevent cancer cells from completing division and will help us design better compounds.

In the synaptic transmission arena we made major advances. With Professor Mike Cousin at the University of Edinburgh, we found that a protein called GSK3 controls dynamin’s function in nerve cells. A surprising partnership between GSK3 and a previously discovered dynamin controller, cdk5, was revealed. GSK3 and cdk5 have previously been linked to bipolar disorder and Alzheimer’s disease. The GSK3/cdk5 partnership exerts control over the rate of nerve cell communication in situations when the nerve cells are highly stimulated — which occurs in epilepsy, mood disorders and early stage Alzheimer’s. Capitalising on this, we have new obtained preliminary evidence that our dynamin inhibitors can reduce synaptic transmission and thus can reduce seizures in epilepsy. In the coming year we will focus on determining how to improve the design of our compounds to ultimately develop a new epilepsy therapy.
The immortalisation process requires specific genes (called tumour suppressor genes), which normally function to prevent cells becoming cancerous, to become disabled. Two genes particularly important in this regard are p53 and p16INK4a. Cancer cells also develop ways of preventing the ends of their chromosomes from shortening. Every time normal cells multiply, their chromosomes (called telomeres) shorten slightly. Eventually the telomeres become so short that normal cells stop any further proliferation. Approximately 10-15% of cancers use a mechanism called Alternative Lengthening of Telomeres (ALT) to avoid telomere shortening, and can be among the most aggressive and difficult to treat.

We aim to uncover enough information about immortalisation to be able to develop drugs that block it, and therefore block the growth of cancers.

Achievements

In a combined project with the Garvan Institute, we studied the sequence of molecular events that alters DNA-protein architecture, allowing the p16INK4a gene to be switched off.

With colleagues at the Kolling Institute and elsewhere in Australia and overseas, we studied ALT in a large number of cases of a very aggressive form of brain tumour – glioblastoma multiforme – and confirmed our earlier finding that the presence of ALT predicts a better, although still very poor, outcome for these patients.

We found that cancer cells commonly have surprisingly large numbers of chromosome ends that are recognised by the cells as being damaged. This is especially true of cells that use the ALT mechanism. We dissected molecular pathways that allow cancer cells to go on dividing despite this damage. ALT-dependent cancers may therefore be particularly amenable to treatments that restore the normal connection between telomere damage and cell ageing or cell death.

Highlights

We found a very unusual form of telomeric DNA in ALT-positive cancer cells. Instead of being a linear double helix, this DNA is circular and partly single-stranded. We developed a test that detects these molecules and showed that it clearly distinguishes cancers that use ALT from those that do not. It can be used as a blood test for ALT cancers, because these unusual DNA molecules are in the blood of patients who have those tumours. When ALT is blocked, the circular DNA disappears rapidly, so we expect to use this test to search for chemical compounds that block ALT and which therefore could be developed into anti-cancer drugs.

Future Plans

These achievements are all steps towards understanding the molecular details of how cancer cells become immortalised. Over the coming year we will continue working towards the ultimate goal of designing anti-cancer treatments that work by blocking immortalisation.

Human genetic material is packaged into chromosomes. The ends of the chromosomes, known as telomeres, are an intrinsic part of our body’s normal defence against cancer. In most of our cells, telomeres get shorter as the cells divide (i.e. as we get older). Cancer cells, on the other hand, almost always find a way to circumvent this shortening and so can divide without limit. Approximately 85-90% of human cancers overcome telomere shortening using telomerase, an enzyme not present in most normal cells. This raises the exciting possibility that blocking telomerase could become an effective and specific therapy for cancer.

There are many gaps in our knowledge of how telomerase works. This not only makes it a fascinating enzyme to work on, but also means that we have much to learn before designing rational telomerase inhibitors.

Telomerase interactions with DNA

Telomerase is able to add multiple “blocks” of telomeric DNA in a repetitive manner. It does this using a “racheting” motion, with several parts of the enzyme maintaining contact with the DNA. The number and location of these DNA “anchor sites” have been the subject of much investigation as one possible avenue to block telomerase activity.

A region at one end of the protein had been proposed as a key telomerase anchor site. We discovered a new function for this region in positioning the DNA molecule in the active site of the enzyme, in preparation for adding more DNA. The protein needs to undergo changes in shape during the “racheting” process, and this region keeps the end of the DNA in the right place during these movements. This work was recently published in Nucleic Acids Research.

Not only does this shed light on the mechanics of telomerase movement, it also suggests that this may be a key target when designing telomerase inhibitors. Our collaborators at St Vincent’s Institute for Medical Research have successfully developed a computer model for this important part of the telomerase protein, and, using computer modelling techniques, have identified 200 small molecules that we are now testing for their ability to block telomerase function.
CMRI employs over 100 research scientists, many young and all energetic, from around the globe working toward a common goal – transforming the health of generations through understanding our biological development and how our genes and cells work, so that better treatments and cures for diseases can be developed.

CMRI cancer researcher and cell cycle expert, Dr Daniel Speidel works in the Cell Transformation Unit and has been with CMRI for four years. Daniel relocated to Australia from Germany and the research he undertakes is focused on enhancing our understanding of how cancer cells can be targeted to prevent cancer growth and spread.

Meet a Researcher: Dr Daniel Speidel
Cell Transformation Unit, CMRI

“There is a tremendous need to develop more effective, specific and less toxic therapeutic approaches to treat cancer and lessen patient suffering. My research focuses on genetic alterations associated with therapy resistance and mode of action of chemotherapeutic treatments. I am proud to work at CMRI which is at the forefront of cancer research.”

Cell Transformation Unit

Cancers are able to multiply indefinitely and overcome normal signals that would otherwise lead to cell death. The Cell Transformation Unit focuses on understanding the mechanisms of cell proliferation, immortalisation and survival. Understanding how these processes are controlled will lead to a better understanding of how cancers form and provide useful information for new anti-cancer agents.

A major focus is the p53 tumour suppressor and how it functions to prevent cancers.

Progress and Achievements

Our team and collaborators at the University of Otago are working on mouse models carrying specific p53 mutations. One such model explores the hypothesis that p53 prevents tumours via apoptosis, a specialised form of cell death. Mice were engineered to lack the apoptosis-inducing region of p53; they became resistant to tumours of T cell origin but eventually developed B cell tumours. Apoptosis is therefore not required to prevent T cell tumours but could contribute to preventing B cell tumours. We are currently investigating other defects in these mice. So far, it appears they are defective in DNA repair, which could also contribute to tumour prevention by p53. Our second model addresses a specific variant (isoform) of human p53 - the first mouse model carrying the D133p53 isoform. Evidence from human tumours suggests it could promote cancer formation, something we have now proven with our model. Continued investigation will determine how this p53 variant contributes to cancer and how to inhibit its effects.

We have also established a powerful new technique (‘In vivo cell cycle analysis’) allowing quick, easy and reproducible assessment of subtle cell cycle alterations in tissue samples, including patient biopsies. Most tissues were not previously accessible for this kind of analysis. The new methodology enables us to investigate specific aspects of cancer formation and therapy that could not be examined before. We will be able to conduct experiments to understand why some organs are more frequently affected by cancer than others and why the efficiency of p53 in preventing cancer varies between different tissues.

Dr Scott Cohen continues his structural and functional studies into the human telomerase enzyme complex. With the help of his collaborators at CSIRO, human telomerase has been over-expressed in 293T cells, and this system has been adapted to make scale-up feasible and cost-effective. With continued optimisation of telomerase expression and further scale-up, Dr Cohen hopes to initiate X-ray crystallisation trials in mid-2011.

Other team members have studied the protein YB-1, which we previously showed could regulate p53 activity. Increased abundance of YB-1 is associated with poor patient prognosis, probably through its ability to stimulate cell growth and confer drug resistance. We and colleagues at the University of Auckland have investigated how YB-1 regulates cell growth and have identified a key cell cycle regulatory pathway that it controls. We have also shown that YB-1 can exist in several phosphorylated forms. We hypothesise that one of these phosphorylated species is oncogenic, resulting in cancer if dysregulated. We are currently cataloguing the different phosphorylated species to define a clearly oncogenic species for use as a prognostic indicator.
Embryology Unit

Embryonic development is orchestrated by genes expressed within the embryo. All are precisely controlled so that they are active in specific locations, participate in specific signalling pathways, and regulate the activities of other genes. The more we understand about their roles, the more we can comprehend the complexities of embryonic development and the congenital anomalies that arise when these genes are disrupted.

Intersection of transcriptional and signalling activity in development

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

Head abnormalities also occur in Saethre-Chotzen syndrome, caused by errors in the TWIST1 gene. We used mouse models to show that loss of Twist1 affects different components of the craniofacial skeleton and the muscles of the face, eyes and jaws. Losing Twist1 function in the limb causes malformations of the fingers and the bones of wrist and forearm due to changes in signalling activity.

Molecular control of gut development

We studied the role of the Rbm47 gene, which encodes an RNA binding protein expressed in the cells lining the gut. Reduced function of this gene in genetic mouse models leads to abnormal differentiation of the gut lining and disrupts its maturation.

We also identified a CDC42-related Rho GTPase that is active in the endoderm, the embryonic tissue that forms organs including the liver, pancreas and thyroid. By lowering the activity of this gene, we showed that it is required for proper cellular organization within the endoderm. Reduced gene function results in an abnormal organization of the epithelium, which appears to be critical for endoderm cells to respond properly to signals from surrounding tissues.

Embryo derived stem cells for studying germ layer differentiation

We have developed a new type of stem cell from mouse embryos poised to undergo germ layer formation. These stem cells can renew themselves in culture and can differentiate into cell types of multiple lineages. Stem cells derived from embryos at different developmental stages display unique patterns of gene activity and lineage potency. We are currently optimising the method to direct the differentiation of these stem cells, and induced pluripotent stem cells generated by reprogramming fully differentiated cells, into gut (specifically liver and pancreas cells) and heart cells. The goal is to test the principle and feasibility of combining cell-based and gene therapy to treat inborn errors of metabolism.

Genetics of eye disorders (Eye Genetics group)

This work aims to discover novel disease genes leading to blindness in humans, allowing us to develop treatments to prevent vision loss. We have undertaken high resolution sequencing approaches to identify several candidate disease genes in patients with eye conditions, including glaucoma, retinitis pigmentosa and corneal disorders. We also investigated mouse models of eye diseases; one of these (with loss of Twist2 function) has revealed the developmental causes of keratoconus, where an abnormally shaped cornea leads to vision impairment.

Molecular basis of Rett Syndrome

Rett syndrome is a debilitating neurological condition associated with mutations in the MeCP2 gene. Our current focus is to identify the genes and proteins that are deregulated in specific brain regions of MeCP2 mutant mice and elucidate their roles in the syndrome. We are also studying an X-linked gene, Cadls, which when mutated causes Rett-like symptoms, generating a genetic mouse model to reduce Cadls function within the nervous system.

Gene Therapy Unit

The Gene Therapy Research Unit (GTRU), a joint initiative of CMRI and The Children's Hospital at Westmead, is dedicated to developing novel gene-based strategies for the treatment of childhood genetic disease.

This partnership provides an excellent environment to undertake the challenging task of translating progress in the laboratory to new therapies in the clinic. While rewarding, this translational journey is immensely challenging as it demands effort across many fronts. In addition to laboratory research activities, we must develop specialised clean-room facilities for the genetic repair of patient cells, clinical grade gene delivery formulations, and standardised procedures governing all aspects of clinical trial activity, while complying with complex regulatory requirements.

Highlights

Over the last year we have played a major role in driving a Westmead Research Hub-wide approach to taking gene and cell therapy research through to clinical application. This effort helped bring a large amount of infrastructural funding onto the campus and led to the establishment of the Sydney Cell and Gene Therapy Centre, consolidating our current cell and gene therapy research through to clinical application.

In addition to the highlights above, laboratory work continues to focus on gene therapy strategies for childhood diseases of the liver and bone marrow. The bone marrow studies underpin our current clinical trial activities while the liver work focuses on the treatment of urea cycle defects. To date we have successfully cured mice with ornithine transcarbamylase (OTC) deficiency, the commonest urea cycle defect, and are working on human liver cells with human clinical trials envisaged in the next 3-5 years. This area is receiving international attention with collaborative links currently being established to help carry it forward.

Ethics

Human clinical trials necessitate in depth consideration of ethical issues. While these have always been an integral part of our translational efforts, Claire Deakin, a PhD student in the GTRU, has brought a more formal interest in this area. Several publications have already resulted and an international survey of how gene therapy researchers perceive and process risk when designing clinical trials is underway.
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 may become contaminated, and such contamination may impact on research 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 Australia 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 quality control to validate 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 large range of authenticated cell lines are readily available for use by Australian scientists.

In addition, CellBank Australia offers a range 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.

In 2010, CellBank Australia became an International Depository Authority under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This means CellBank Australia can now provide secure storage for human and animal cell lines and hybridomas that are the subjects of patent applications.

In 2010, CellBank Australia received 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. Its full name is The Lady Mary Fairfax CellBank Australia and it was established in 2005 by a joint venture of the Children’s Medical Research Institute (CMRI), Cure Cancer Australia Foundation, and the National Breast Cancer Foundation. It has been independently operated by CMRI from July 2007.

In the last two years, CMRI has undertaken an extensive program of refurbishment and expansion of its Proteomics Facility and has secured the means to initiate the development of The Centre for Kinomics (CFK) – a joint venture of CMRI (proteomics) and the University of Newcastle (UoN) (medicinal chemistry).

CFK is a new, Australian-first, large, non-commercial initiative which builds upon demonstrated research excellence, leadership and successful collaborations, between proteomic experts from CMRI and medicinal chemists from UoN. CFK, equipped with state-of-the-art instrumentation and expert personnel will provide an entirely new approach to the understanding of therapeutic drugs and ways to improve them.

Generous funding from Ramaciotti Foundation and Australian Cancer Research Foundation (ACRF) has supported the establishment of CFK with grants of $1 million and $3.1 million, respectively, for the purchase of three cutting edge mass spectrometer (MS) and other systems to be housed on both campuses.

Further funding received from Cancer Institute NSW (CI NSW), Australian Research Council Linkage, Infrastructure, Equipment and Facilities scheme (ARC LIEF), and Ian Potter Foundation have been used for the purchase of two advanced MS systems, dedicated to important research projects requiring a phosphoproteomics approach or proteomic data.

The Facility currently houses six instruments, with the last two scheduled for purchase in mid 2011. This has resulted in vastly increased capacity, quality and productivity, all required to meet the demand for our expertise within CMRI, Australia and internationally. The expansion was absolutely vital for the core team to continue their groundbreaking discoveries and to maintain their leadership in the field.

Our main focus at present is to facilitate a smooth and successful 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. Our priority is to ensure that these facilities realize their full potential to enhance Australian science.

**Need To Know**

**What is Mass Spectrometry?**

Mass Spectrometry (MS) is the single most powerful analytical technique that underpins all modern day biomolecular science. It measures molecules to determine their weight thus facilitating the identification and characterization of key components in biological processes (proteins, peptides, carbohydrates, DNA, drugs). MS is the best approach to the analysis of the signalling events (e.g. protein phosphorylation) that drive these processes within cells.

**What is Kinomics?**

Cellular signalling is largely controlled by protein kinases, which direct phosphorylation-based signalling. Approximately 200 kinases are present in any one cell or tissue at any one time, making up the cellular “kinome”. Kinomics is a new discipline allowing us to explore the cellular kinome in a rapid, systematic and global way. Comprehensive analysis of the kinome will improve our understanding of cell signalling and identify therapeutically relevant kinase targets for drug discovery.
Meet a Volunteer: Diana Mahony
CMRI Volunteer and President and Secretary, Judith Hyam Memorial Trust Fund For Cancer Research

“Cancer research is important to me because cancer has affected a number of people close to me and my family. I enjoy volunteering at CMRI because it enables me to support the researchers here and contribute to the local Parramatta community”

Volunteers are an invaluable resource for CMRI and their contribution directly impacts the success of our fundraising, marketing and administration activities.

Mrs Diana Mahony is a long time supporter of CMRI both as a regular volunteer in our administration team and through her role as the President and Secretary of the Judith Hyam Memorial Trust Fund for Cancer Research. Diana’s energetic and community-spirited support of the Institute’s work is truly inspiring.

Over the past 20 years approximately $1.5 million dollars have been raised for the CMRI Cancer Research Unit through the efforts of Diana and the members of the Judith Hyam Memorial Trust Fund for Cancer Research.

CMRI congratulates Diana Mahony on being honoured by Parramatta City Council as the 2011 Australia Day Senior Citizen of the Year, for her enormous contribution to cancer research.

Fundraising
CMRI is an independent institute able to pursue long term research goals funded by a national community of supporters and Jeans for Genes® campaigns. Over half of our income comes from private fundraising sources, including from an endowment fund established more than 50 years ago.

The photo above shows Nobby Alcala enjoying a happy, healthy and full life. However, just a few years ago Nobby’s health prognosis was not good. At just 2 years of age Nobby was diagnosed with a type of cancer called neuroblastoma. This cancer kills half of the children who develop it, and for Nobby the threat was compounded by the fact he was already at Stage 4 (the worst stage) when he was diagnosed by doctors at Westmead Children’s Hospital. Thankfully, today Nobby is in remission and the Alcala family from Sydney has become important supporters of CMRI. The Alcala family is just one example of why supporting medical research is a vital investment that will benefit Australian families for generations to come.

It is with great thanks to the ongoing support of the Australian community that the CMRI fundraising program has experienced a successful 18 months despite the challenging financial climate. The following pages highlight and acknowledge the people and activities that are CMRI’s fundraising program. The annual fundraising income and expenditure is presented in the Financial Management section of the 2010 Report on page 28.
CMRI Redevelopment Campaign

CMRI has initiated plans for a redevelopment on our existing site to provide us with the space and requirements needed to expand our research outputs and allow for future growth. With more scientists contributing their skills to our research endeavours we can accelerate and expand our research capacity, create greater breadth in our core areas, and grow our international reputation. This will also ensure that research leaders remain in Australia, contributing to our nation’s scientific achievements and long term medical advancement.

To achieve our vision of growth, CMRI has plans to redevelop its building from its current two storeys to an eight storey building. Our proposed redevelopment is part of ongoing development plans for the whole of the Westmead research precinct (see diagram pictured above), all of which will create a world-leading centre for research facilities. Most importantly, by expanding our laboratory space and capabilities, we will be able to maximise our research potential and take our discoveries to the next level for the benefit of our children and their families.

CMRI is working with State and Federal Governments and existing supporters to secure funding for this project. Note: In May 2011 NSW State Government announced a $20 million funding grant to support CMRI redevelopment plans.

Major Supporters and Partners

We again acknowledge the ongoing support of a wide range of individuals, businesses and trusts and foundations.

Our corporate partners are an important part of our fundraising program and CMRI is fortunate to have long standing relationships with a number of companies.

We give special thanks to Kimberly-Clark Australia who continued their support of a named Research Fellowship (Kimberly-Clark Australia supporting Dr David Loebel in our Embryology Research Unit), plus financial support of our Jeans for Genes campaign.

Mr James Fairfax continues his generous support of our Embryology Research Unit and we also acknowledge the long term support from the Judith Hyam Memorial Trust Fund for Medical Research whose generosity has enabled the continuance of three named positions in our Cancer Research Unit.

We pride ourselves on developing long term mutually beneficial relationships with all our supporters and partners. Please refer to the 2010 Report Addendum available on the CMRI website for a list of all CMRI major supporters.

Bequests

CMRI continues to receive bequests from a wide range of people, many of them having experienced firsthand the tragedy of childhood illness. The generosity of these benefactors will help us protect future generations of children and families from pain and suffering. Bequests are an important way we can grow CMRI’s endowment fund.

CMRI website for a list of all CMRI major supporters

Community Fundraising

CMRI is very grateful for the support of the many community groups and individuals that generously support our programs and raise funds for the Institute.

Throughout the 18 month period community supporters have hosted a wide range of fundraising activities for CMRI including morning teas, merchandise sales and events such as Golf Days. The community also generously supported the CMRI direct mail donation appeals in 2009 and 2010.

We thank our wonderful CMRI committees who continue to be the foundation of our community fundraising and public awareness efforts.
Meet a Committee: Racquet Committee

Mrs Prue Kellaway, President, Racquet Committee

“Scientific research is not possible without the long term commitment and dedication of the researchers. The tireless efforts of scientists that lead to discoveries are often unheralded. I feel privileged to help raise awareness and funds for such an immensely worthwhile cause because our future is our healthy children.”

Our network of committees is a critical part of CMRI fundraising at a local level and represents the heart and soul of the Institute. CMRI has 25 committees located across Australian Capital Territory and New South Wales which raise vital funds for the various research programs being undertaken at CMRI.

Mrs Prue Kellaway is President of the Racquet Committee based in Sydney’s Pymble and has been a supporter of CMRI for more than 40 years. Prue’s involvement with CMRI began in the Institute’s founding years at Royal Alexandra Hospital for Children where she was training to become a registered nurse. Prue joined the Springtime Committee (no longer in operation) and later, together with friends went on to form the Racquet Committee which still meets once a week in Pymble after two decades in operation. Still full of enthusiasm, the members of the Racquet Committee and their tennis days are as legendary as the funds they raise each year. Prue is a true champion of scientific research and her ongoing support of CMRI has been invaluable.

Governance and Finance

CMRI is an independent research institute committed to unlocking the mysteries of childhood disease. Based in Westmead, NSW, the Institute employs around 150 people, including over 100 full-time scientists and PhD students, with the balance comprising operational and administrative support staff and a team of fundraisers. The organisational structure of CMRI reflects its corporate governance and areas of responsibility. CMRI is very proud to have received the ‘Excellence in Administration and Financial Management’ at the Suncorp Western Sydney Awards for Business Excellence in 2010.
Leading the management of CMRI is a Board of Directors which consists of ten independent non-executive directors and one executive director. Combined, the Board brings a wide range of business and commercial skills to CMRI, spanning numerous industries and sectors.

The role and responsibility of the Board is to identify the critical aspects of organisational governance and to manage the overall business and affairs of CMRI.

The names of directors in office:
- Professor Frank Martin MB BS FRANZCO FRACS AM, President [Pic 1]
- Mrs Carolyn Forster OAM, Vice President [Pic 2]
- Mr Rod Atfield FIA FIAA FAII, Treasurer [Pic 3]
- Mr John Bevins [Pic 4]
- Professor Ian Caterson MBBS BSc(Med) PhD FRACP [Pic 5]
- Mr John Dunlop AM [Pic 6]
- The Hon Craig Knowles [Pic 7]
- Professor Kathryn North MD BSc(Med) FRACP [Pic 8]
- Mrs Patricia Payne OAM MPS PhC [Pic 9]
- Professor Roger Reddel BSc (Med) MBBS PhD FRACP FAA, Director CMRI [Pic 10]
- Clinical Professor Graeme Stewart AM BSc(Med) MBBS PhD FRACP FRCPA [Pic 11]

The names of resigned directors:
- Dr Tom Parry AM BEd MEd PhD [resigned December 2010]
- Mr Christopher Cullen AM ED BE FAIM [resigned November 2009]
- Ms Elizabeth Hallett LLB BComm [resigned December 2009]

Under the Constitution of CMRI, Board members are elected or appointed for three year terms and officer positions are voted on annually.

More details regarding the directors including their biographies and qualifications can be found in the 2010 Report Addendum available on the CMRI website.
The Organisation

CMRI Board of Directors

Intellectual Property Committee
Audit & Risk Committee
Finance & Investment Committee
Nominations & Remuneration Committee

Operations
Research
Specialised Facilities
Executive
Fundraising

- Lab Management
- Bio Services
- Building Facilities
- Information & Communications Technology
- Cancer Research
- Cell Biology
- Embryology
- Gene Therapy
- Cell Signalling
- Cell Transformation
- CellBank Australia™
- Biomedical Proteomics Facility (including ACRF Centre for Kinomics™)
- Director's Office
- Finance
- Human Resources
- Commercialisation & Affiliations
- Marketing & Communications
- Supporter Services
- Jeans for Genes®
- Community Fundraising
- Philanthropy & Major Partnerships
- Bequests
- Building Redevelopment

MANAGEMENT AND OPERATIONS COMMITTEES

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

Scientific Advisory Centre for Kinomics™
Scientific Advisory CellBank Australia™
Cancer Consumer Panel
Fundraising

Financial Management

The financial highlights of CMRI for the past 18 months are provided below. All numbers are drawn from the audited financial statements of comprehensive income for the year ended 30 June, 2010 and the six months ended 31 December, 2010 and related balance sheets.

Research Grants and Research Income

The Institute continues to successfully compete for grant funding from Australian Commonwealth Government programs, New South Wales Government programs and from private Trusts and Foundations in Australia and internationally. In this 18 month period, successful grant applications yielded $16,000,000 of income for the Institute’s research programs. Grant income is expended on research projects and personnel, approved research equipment and necessary infrastructure costs.

Investment Income

The Institute holds a long term view of investing its financial assets, balancing risk and return across a diversified portfolio of investments. The Finance and Investment Committee adopts a strategic asset allocation model and utilises the expertise of specialist fund managers and independent investment advisors. The Global Financial Crisis in 2008/09 significantly impacted the market value of our investments and also the earnings generated by them for the year ended 30th June 2009. In the 12 months ended 30th June, 2010, earnings continued to be depressed although market values began to recover. In the following 6 months ended 31 December, 2010, earnings have improved and market values were overall sustained. In this 18 month period, our endowment fund provided approximately $12,000,000 of investment income for use by the Institute.

Fundraising Income

Our fundraising activities comprise a number of streams, including direct mail; sale of merchandise; regular giving programs; online donations; bequests; donations from private funds, trusts and foundations; activities and events run by our community committee networks; and our major fundraiser, the Jeans for Genes® campaign. Gross fundraising revenue for the 18 months to December 2010 amounted to $12,000,000. Jeans for Genes continues to be our flagship campaign, raising $6,000,000 in the 18 months period. The bulk of this revenue comes from our networks of volunteers on Jeans for Genes Day, schools, business and Australian communities, who purchase merchandise, fundraise or donate. In addition, our annual Gala Dinner attracted much interest for the auction of celebrity jeans painted by well known Australian artists.
Meet a Student: Zeenia Kaul
PhD Student, Cancer Research Unit

“Working at CMRI has provided me with invaluable experience in multidisciplinary scientific research and I feel very fortunate to have worked with some of the greatest minds in science today. The skills and new friendships that I have developed at CMRI are irreplaceable.”

Children’s Medical Research Institute selects some of the finest PhD students from around Australia and the world, to contribute to its vital research programs. Students undertake training and have gained various awards and degrees under the guidance of CMRI researchers.

PhD student Zeenia Kaul moved to CMRI from Japan in February 2008 and works in the Cancer Research Unit under the supervision of Prof. Roger Reddel. In 2010, Zeenia was first selected by the Australian Academy of Science and then by the Council for Lindau Nobel Laureate Meetings as one of the ten Australian students to attend the meeting in Lindau, Germany. The annual Lindau meetings are a globally recognised forum for the exchange of knowledge, ideas and experiences between Nobel Laureates and young researchers.

During her time with CMRI, Zeenia has also received a Research Scholar Award from the Cancer Institute NSW, an Australian Postgraduate Award, the Judith Hyam Memorial Trust Fund for Cancer Research Scholarship, and several other prizes and awards.

Zeenia’s research is an important part of the Cancer Research Unit’s efforts to understand the cellular and molecular processes underlying cancer, and to lay the foundations for developing new forms of cancer treatment.
## Financial Summary

### Profit and Loss Statement

<table>
<thead>
<tr>
<th></th>
<th>6-months</th>
<th>12-months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dec 2010</td>
<td>Jun 2010</td>
</tr>
<tr>
<td></td>
<td>in $ '000s</td>
<td>in $ '000s</td>
</tr>
<tr>
<td><strong>Revenues</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research</td>
<td>5,921</td>
<td>9,961</td>
</tr>
<tr>
<td>Fundraising</td>
<td>5,429</td>
<td>6,766</td>
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<tr>
<td>Investments</td>
<td>2,834</td>
<td>4,191</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>14,184</td>
<td>20,918</td>
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<tr>
<td><strong>Expenses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research</td>
<td>8,144</td>
<td>13,697</td>
</tr>
<tr>
<td>Fundraising *</td>
<td>1,956</td>
<td>3,139</td>
</tr>
<tr>
<td>Administration and facilities</td>
<td>2,690</td>
<td>4,410</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12,790</td>
<td>21,246</td>
</tr>
<tr>
<td><strong>Surplus/(loss) before investment transactions</strong></td>
<td>1,394</td>
<td>(328)</td>
</tr>
<tr>
<td>Investment transactions, net</td>
<td>41</td>
<td>148</td>
</tr>
<tr>
<td><strong>Surplus/(loss) from continuing operations</strong></td>
<td>1,435</td>
<td>(181)</td>
</tr>
<tr>
<td>Other comprehensive income from Available-for-sale financial assets</td>
<td>342</td>
<td>4,562</td>
</tr>
<tr>
<td><strong>Total comprehensive income for the period</strong></td>
<td>1,778</td>
<td>4,381</td>
</tr>
</tbody>
</table>

* includes Building Redevelopment Campaign Costs of $385,000 for June 2010 and $219,000 for December 2010

### Balance Sheet

<table>
<thead>
<tr>
<th></th>
<th>As at:</th>
<th>31 Dec 2010</th>
<th>30 Jun 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>in $ '000s</td>
<td>in $ '000s</td>
</tr>
<tr>
<td><strong>Assets</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Current Assets, including cash &amp; term deposits</td>
<td>8,598</td>
<td>7,516</td>
<td></td>
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<tr>
<td>Other Financial Assets</td>
<td>66,465</td>
<td>66,277</td>
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<tr>
<td>Property, Plant and Equipment</td>
<td>15,223</td>
<td>14,660</td>
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</tr>
<tr>
<td>Other Non-current Assets</td>
<td>1,101</td>
<td>973</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>91,387</td>
<td>89,426</td>
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</tr>
<tr>
<td><strong>Liabilities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Liabilities</td>
<td>3,863</td>
<td>3,670</td>
<td></td>
</tr>
<tr>
<td>Non-current Liabilities</td>
<td>259</td>
<td>268</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4,122</td>
<td>3,938</td>
<td></td>
</tr>
<tr>
<td><strong>Net Assets</strong></td>
<td></td>
<td>87,265</td>
<td>85,487</td>
</tr>
</tbody>
</table>

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

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**Thank You**

On behalf of everyone at CMRI, we would like to thank the Australian community and our research, business and corporate partners for the ongoing support we receive. With the support of these networks, we can continue to work toward our singular aim of advancing the prevention and treatment of disease, leading to healthier generations of children.

From all of us at CMRI
These 4 chemicals are the building blocks of DNA, the basis of life...

ATCG

- Adenine
- Thymine
- Cytosine
- Guanine

...and the basis of our research