Why are we what we are?

Healthier kids, brighter futures

Children’s Medical Research Institute
2011 Annual Report
DNA stands for DeoxyriboNucleic Acid – a molecule that forms a double helix and acts as the blueprint for living things.

1 in 20 children worldwide suffers from a birth defect or genetic disease, and Children’s Medical Research Institute (CMRI) is dedicated to changing this by advancing the treatment and prevention of childhood diseases.

CMRI pioneered microsurgery, immunisations against lethal childhood illnesses and care for premature babies, all of which has improved the lives of countless Australian children over the last 50 years. Today, CMRI is the site of world-leading research in areas such as cancer, neurobiology, embryology and gene therapy.

CMRI collaborates with scientists all over the world to push research forward. It also provides important resources for scientists in 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.

CMRI is a founding member of the Westmead Research Hub, a major medical research precinct, uniting the efforts of local scientists to perform at a national and international level. The Institute employs more than a hundred full time scientists and educates dozens of PhD students (the ground-breaking scientists of the future) through its academic ties to the University of Sydney.

CMRI’s achievements are made possible by a network of devoted community supporters, as well as the iconic Jeans for Genes™ fundraising campaign.

Welcome to our annual report highlighting our achievements over the calendar year, January through December, 2011 and our aims for 2012 and beyond.
Children’s Medical Research Institute has its eye on the future and in 2011 began positioning itself for growth. The institute has endured over 50 years of changing economies and financial markets, benefitting from the endowment fund first set up by Sir Lorimer Dods in 1958, and was able to weather the adverse financial climate. At the same time, CMRI continued to grow its scientific research and announced several important discoveries and developments.

Each of our established research units has made great strides over the last twelve months. Their key achievements for 2011 are set out in this annual report. I draw particular attention to the establishment of a new research unit—the Cell Cycle Unit—headed by Dr. Megan Chircop. This new unit builds on our strong cancer research presence. We also finalised our plans for the ACRF Centre for Kinomics, an Australian first, and have established a specialist Bioinformatics Unit.

We recently received the $20 million capital grant promised by the NSW government and have made the decision to commence our building expansion. After completion of detailed designs, we expect to commence construction later this year or in early 2013. This is the first stage of approved plans for a major redevelopment of the site. This redevelopment will not only expand our research facilities, providing more opportunities for discovery and increased research output, but it will also showcase a new facility for developing therapeutic drugs that will benefit cancer research across Australia.

As ever, we are indebted to our fundraising committees whose tireless efforts and devotion to CMRI have made our continued growth possible. Our volunteers were recognized at a special ceremony held at Government House last October by Governor-General Ms. Quentin Bryce AC, where Her Excellency expressed her appreciation for their contribution to our nation.

In addition to our community supporters, the iconic Jeans for Genes fundraising campaign is another key reason CMRI is well placed for expansion. The campaign was established in 1994 and has helped to substantially grow our endowment fund over the years. 2011 was a challenging year for fundraisers. Competition for attention is always increasing and a series of natural disasters pulled strongly on the public’s goodwill. However, we are very excited about our 2012 campaign and some of its new ideas and the new supporters coming on board.

We established a new Marketing & Communications department in 2011, which conducted a brand research study and designed a new marketing and communications strategy for 2012. This will capitalize on the investments CMRI has made over the past two decades in building such a widely recognized brand as Jeans for Genes and will also bring greater exposure to the cause of CMRI.

On behalf of the Board, sincerest congratulations must go to CMRI Deputy Director, Professor Patrick Tam, who was honoured on the international stage in 2011. Professor Tam was inducted into the Royal Society of London and joined a select membership that includes such great minds as Sir Isaac Newton, Albert Einstein and Charles Darwin.

Our Director, Professor Roger Reddel, received an award from Cancer Institute NSW naming him “Outstanding Cancer Researcher of the Year in 2011” for his contributions to cancer research. The Board continues to be privileged to have a Director with the knowledge and insights of such a world-class scientist to steer its research development and growth in the years ahead. We also congratulate Board member Professor Kathryn North on achieving Australia Day Honours this past January.

Finally, I would like to thank all the people who are working hard for our success. Our Board Members continue to contribute time and energy to this fantastic cause. CMRI’s outstanding record of scientific achievement would not be possible without the dedicated scientists and research students who devote each day to understanding and finding ways to treat childhood disease. We thank them for their ongoing efforts. I would also like to thank the management, administration and staff of CMRI who support the scientists and their work behind the scenes.

Thanks to everyone’s contributions, and especially our generous supporters, CMRI is taking advantage of its enviable financial position and history of scientific achievement to break new ground in the year ahead.

Frank Martin
President
May 2012

Children’s Medical Research Institute continues to do world-leading research in the areas of neurobiology, cancer, birth defects and gene therapy. This year was our most successful ever in terms of scientific recognition for the work of the Institute. More details are given in the Addendum to the annual report, but I will highlight a few of the Institute’s accomplishments here.

Professor Patrick Tam, head of the Embryology Unit, received the FRS and other recognition for his work over the years, which continues to be groundbreaking. In 2011, he and his team discovered how a key protein is involved in head and brain development. The Cancer Research Unit also received several awards and commenced a new period of funding from Cancer Council NSW, which has generously committed a further $2.25 million over five years to work that is expected to result in new types of treatment for some of the cancers that are currently most difficult to control.

The Gene Therapy Unit has made advances towards treating inherited liver disease, with clinical trials expected in just a few years. The Cell Signalling Unit identified a control point for nerve cell branching which is very important for our understanding of brain development, and their exciting work on the dynamin proteins is progressing steadily towards drug treatments for cancer, epilepsy and infectious diseases.

CMRI is committed to analysing the fundamental processes of life - and what goes wrong in disease - as the basis for making major advances in treating childhood disease. This is what continues to drive us. The medical advances that have been made in research laboratories around the world within the past few generations have been truly outstanding, but I am convinced that we have barely scratched the surface of what it is possible to achieve. It is essential now that we provide the resources necessary to “translate” discoveries made at CMRI into treatments that directly benefit children.

For that purpose, we have begun a building re-development that will expand our research facilities and capabilities. We are very fortunate that the NSW State Government has endorsed our plans for the future by contributing very substantially to expanding our facilities. This will allow us to begin construction of new facilities and, more importantly, to start increasing our research efforts.

The recent establishment of the Cell Cycle Unit, which also focuses on developing cancer treatments, is an indication of what is to come. Our strategy is to build on our existing research strengths, providing a concentration of scientists working together on specific problems with complementary skills and ideas to solve problems that have previously been too tough to tackle. Our new Bioinformatics Unit will provide a much needed resource, enabling us to better understand and deal with the vast quantities of research data that are now generated by our research groups.

Biomedical Proteomics continues to be a central resource for research throughout the Institute and beyond, and with support provided by the Ramaciotti Foundations and the Australian Cancer Research Foundation, the ACRF Centre for Kinomics is poised to launch CMRI and Australia to the forefront of new areas of cancer research. This new facility will provide innovative technologies to aid rapid development of medicines for a wide range of diseases, including epilepsy and cancer. The centre is well on track to open its doors for use by researchers across Australia in late 2012, and is one of the many facets of CMRI research that will greatly benefit from the additional laboratory space available in stage one of our building redevelopment.

The tremendous success of biomedical research so far has been built on cooperation and collaboration on a global scale. CMRI shares resources and ideas with researchers locally, nationally, and internationally. CMRI is a founding member of the Westmead Research Hub, which coordinates purchase and use of expensive research equipment on this campus, maximising the value of every dollar donated to research. We are delighted that our partners at Westmead Millennium Institute have already commenced the process of relocating their research facilities directly adjacent to ours. Together with researchers at Children’s Hospital Westmead, we are creating a major research precinct that will be tremendously beneficial to the people of Western Sydney and beyond. CMRI is also a founding member of the Kids Cancer Alliance, which has funding from Cancer Institute NSW, the University of Sydney, and will encompass almost all of the paediatric cancer doctors and researchers throughout NSW. This alliance will speed up the development of new treatments for children suffering from a range of cancers.

CMRI relies on its strong links with researchers in Westmead and other external collaborations. But none of our successes would have been possible without equally strong links to our extraordinary community of supporters. As CMRI works towards the future, we continue to rely heavily on the enduring relationships developed over the last 50 years, and to seek out new partners who share our goals.

Roger Reddel
Lorimer Dods Professor and Director
May 2012

Report from the President

“CMRI is taking advantage of its enviable financial position and history of scientific achievement to break new ground in the year ahead.”

President: Frank Martin

Report from the Director

“The medical advances that have been made in research laboratories around the world over the past few generations have been truly outstanding, but I am convinced that we have barely scratched the surface of what it is possible to achieve.”

Director: Roger Reddel
CMRI conducts the ‘basic’ research that allows us to understand the fundamental causes of a range of disorders, such as cancer and epilepsy. This crucial foundation is needed if we are to find ways to treat or prevent these diseases. We are also dedicated to going beyond basic research, by translating the discoveries made in the laboratory into new treatments for patients through our gene therapy and drug discovery programs.
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 Genetists & Ophthalmologists throughout Australia and New Zealand
• CSIRO Division of Health Sciences and Nutrition, Parkville VIC
• CSIRO Materials Science & Engineering, Parkville VIC
• 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 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 Massachussets, USA
• University of Washington, Seattle WA, USA
• Wake Forest University, Wake Forest NC, USA
**Research Areas**

**Telomere chromatin in ALT**

We are investigating many aspects of telomere chromatin structure and telomere biology, including telomere length trimming and telomeric DNA sequences. Our aim is to understand how ALT telomeres are structured and how they differ from telomeres in normal and telomerase-positive cells. This will help us to understand the ALT mechanism in more detail and provide information on possible targets for interfering with ALT activity in cancer cells.

**Genes involved in ALT**

The C-circle assay for detecting ALT activity, which was developed by Jeremy Henson in our laboratory, has enabled us to search for the genes that repress ALT in normal cells. We are also using this and other techniques to find the genes needed for ALT activity. These studies will enable us to find targets for the development of ALT-inhibiting therapeutic drugs to treat cancer.

**ALT in normal tissues**

We have developed a way to detect ALT activity in mouse tissues by demonstrating that a DNA sequence introduced into the telomere can be copied from telomere to telomere. We are developing this technology to further study how low levels of ALT activity can become sufficiently elevated to prevent telomere shortening and allow unlimited proliferation of cancer cells.

**STC**

There is excessive activity of the stanniocalcin genes (STC1 and STC2) in many types of cancers. We have found that STC1 is involved in key pathways that respond to oxidative stress. Our current studies are focused on the role the stanniocalcins play in allowing cancers to invade normal tissues and spread throughout the body.

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**Highlights**

The accomplishments of the CRU were recognised by the research community on many levels in 2011. Researcher, Axel Neumann, shared the University of Sydney’s Peter Bancroft Prize for his studies showing that there is a normal member of the ALT mechanism in mice, and CRU Unit Head, Roger Reddel, received the Premiers’ Award for Outstanding Cancer Researcher of the Year 2011. In addition, the C-circle assay, which measures ALT activity and which was developed by the CRU as a blood test for detecting cancer, has now been licensed for research use in the USA.

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**The Cell Biology Unit (CBU)**, headed by Associate Professor Tracy Bryan, is dedicated to understanding the protein telomerase, which is used by 85% of all cancers in children and adults. The cancer cells use telomerase to keep growing uncontrollably, thus it is a key target for cancer treatments, which are predicted to have fewer side effects than current radiation and chemotherapy. The Cell Biology Unit aims to understand the structure and behaviour of telomerase in unprecedented detail in order to rationally design better anti-cancer drugs.

**Telomerase interactions with DNA**

The functions of different regions of the telomerase molecule are just starting to be understood. A region at one end of the protein had been proposed as a key site of interaction with telomeric DNA. We discovered a new function for this region in positioning the very end of the telomere in the heart of the telomerase enzyme, in preparation for adding more DNA. The protein needs to undergo changes in shape during telomeric DNA addition, and this region of the telomerase protein keeps the end of the DNA in the right place during these movements. This work was 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.

One proposed method to block telomerase action is to “lock” the end of the telomere into a folded-back structure called a G-quadruplex. It has been thought that telomerase cannot extend these structures; however, we found that a particular subset of G-quadruplexes can be extended by telomerase. We hypothesise that molecules that lock G-quadruplexes will nevertheless be functional at blocking telomerase. We are testing this hypothesis, and developing new G-quadruplex blocking molecules, together with the laboratory of our collaborator Dr Jennifer Beck at the University of Wollongong. We plan to test the effects of these molecules on the growth of cancer cells in culture.

**Telomerase movements throughout the cell**

Telomerase consists of several proteins and RNA molecules. The way in which these sub-units are assembled and then taken to the telomere is complex and not fully understood. We have developed two complementary methods to detect telomerase at the telomere in live human cells - not an easy task due to its extreme rarity, even in cancer cells. We found that small structures within the cell called Cajal Bodies are an important stop-over point for telomerase on its way to the telomere. A protein called TCAF1 is known to transport telomerase to Cajal Bodies; we found that TCAF1 plays an additional important role in taking telomerase all the way to the telomere. We continue to explore the proteins at the telomere that are involved in recruiting telomerase at the right time, with the hope of being able to eventually block this process.
The Cell Cycle Unit (CCU), headed by Dr Megan Chircop, was established in July 2011. The major focus of the CCU is to precisely define the mechanisms regulating mitotic cell division. Understanding the molecular regulation of mitosis will provide important insight into cancer biology mechanisms. Dr Chircop has previously identified key proteins involved in mitotic progression and characterised how these proteins function in this process. Current research focuses on understanding the network of proteins required for mitosis and how they cooperate. This will provide insight into the errors that occur during cell division that can contribute to the development of cancer.

"Understanding the complex process of mitotic cell division is fundamental to our understanding of how cancers develop."

Megan Chircop

Research Areas

Basic research: molecular mechanisms of mitosis

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. 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.

The CCU discovered that several proteins in the "SNX family" are required for mitosis. In their recent research findings in 2011, including the discovery that dynamin 1 actually has two endophilin binding sites: a major binding site in a different position in the dynamin I long variant. Each interacts with endophilin independently, yet endophilin can only engage one site at a time. This is surprising, similar mechanisms also control the last stage of cell division cycle. One way these are connected is called endocytosis – whereby cells internalize signals or nutrients from the outside. Many genes are required for endocytosis, but the master regulator is dynamin. Of the three dynamin proteins in the body, the CSU studies dynamin I (dynl1) and dynamin II (dynl2). Dynamin continues to reveal multiple functions, and cells have complex mechanisms they use to restrict dynamin’s activity. The unit also studies proteins that act in endocytosis, including clathrin and syndapin I. In their translational research program, the CSU’s understanding of endocytosis has led to the development of small molecules that could potentially treat epilepsy, kidney disease and some infectious diseases. Although early days, this is an ambitious, long-term program aimed at capitalizing on the CSU’s scientific discoveries to ultimately develop new disease treatments.

"Understanding how endocytosis occurs and is controlled is now helping us develop potential new therapies to control nerve communication and, hence, control diseases such as epilepsy."

Phil Robinson

Highlights

Even though the Cell Cycle Unit is new, it has already developed and tested a range of drugs targeting a critical mitotic protein and demonstrated that these drugs have anti-cancer properties. A major CCU program involves performing preclinical testing of these drugs in mouse models of cancer to reveal the most effective compounds that could be taken forward to human clinical trials.

Calcineurin

Calcineurin We aim to understand the molecular mechanism of synaptic vesicle endocytosis (SVE), an important method of nerve cell signalling, by understanding how phosphorylation (the addition of a phosphate molecule to a protein) affects larger protein-protein interactions. Dynamin I has two splice variants, long or short. We discovered that the calcineurin protein selectively docks with the dynamin I short splice variant to regulate bulk endocytosis, which is used during periods of intense nerve cell activity, like epileptic seizures.

Endophilin

Phosphorylation of particular sites within dynamin I (called Ser-774 and 778) blocks recruitment of syndapin, but not endophilin, which binds to the same site. We mapped the endophilin-binding sites and, surprisingly, found that dynamin I actually has two endophilin binding sites: a minor binding site at the previously known site, but also a major binding site in a different position on the dynamin I long variant. Each interacts with endophilin independently, yet endophilin can only engage one site at a time. This is important information for designing drugs to selectively interfere with these interactions, which may allow us to more finely tune the treatments we are developing for kidney disease and other conditions.

The nerve terminal phosphophosphate

Since SVE is a calcium-triggered process, we proposed that the fastest route to discovering which proteins are important to this process and how they function is to identify the phosphorylation sites (aka phosphorylons) in each of the SVE proteins that rapidly respond to calcium stimulation. So far, we have identified >400 unique phosphorylates on over 160 proteins using our novel pull-down procedure to capture the major
SVE and related proteins. In addition, we successfully revealed the calcium-sensitive subset of phosphosite sites. Bioinformatics has helped to reveal exciting new findings, providing us a handle on the different signalling pathways. Furthermore, we completed an extensive analysis of the phosphorylated SVE proteins from cdk5-knockout mice using mass spectrometry. Cdk5 is an important signalling molecule involved in many cellular processes, but has recently been implicated in a range of neurodegenerative diseases like Parkinson’s and Alzheimer’s. We found a subset of proteins that are potential cdk5 substrates, which will help us understand how cdk5 is involved in these disorders and potentially lead to new avenues of treatment.

**Dynamin drug discovery**

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 many new classes which we call the dynoles, the iminochromones the phthaladyns and the dyngos. 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 series of exciting studies 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.

**Dynamin function in actin dynamics**

In order for dynamin to perform its role in endocytosis, it needs to form into a helical structure around the necks of endocytic vesicles. These helices are polymerized from free dynamin molecules and can also self-assemble into rings that are 40 nanometres in diameter (about 30 molecules) of unknown function. Ring Stabilizer compounds are small molecules that affect dynamin’s activity that we have discovered and patented. These compounds have two unique actions compared with dynamin inhibitors: they stimulate dynamin activity by promoting ring assembly, and they prevent rings from disassembling. This produces prolonged and sustained activation of dynamin. We aim to uncover the cellular mechanisms underlying our novel Ring Stabilizers and develop them as future therapeutics for treatment of proteinuric kidney diseases.

**Q)** How many ‘letters’ make up the instructions for a human?  
**A)** 3,000,000,000

**Meet a Researcher**

 Associate Professor Robyn Jamieson leads the Eye Genetics Group. Her research focuses on diseases that cause retinal degeneration, one of the most prevalent causes of blindness, affecting approximately 1 in 3000 people, both children and adults.

“Some retinal diseases occur in childhood,” Robyn says, “while others develop in adulthood. All have a profound impact on the individual and on society, with significant attendant costs. The associated visual impairment is irreversible, currently untreatable, generally worsens with age, and frequently leads to complete blindness.

“For some cases of retinal disease, there are significant new advances in treatment, with improvement in vision reported after trials using gene therapy. In order for patients to access these potentially sight-restoring trials, and for scientists and doctors to develop new therapeutic strategies, we need to know more about the underlying genetic error in patients.”

Robyn works closely with patients at the Children’s Hospital Westmead and has already discovered 12 genes that cause retinal degeneration and other eye disorders, but she’s aware that there are many more. She now aims to identify additional genetic causes of retinal degeneration using a new technique called Next Generation Sequencing, where every gene in an individual can be sequenced at once. This research, combined with studies of how the affected genes and proteins work, will allow her to find new ways to prevent or cure blindness.

“Blindness and impaired vision are extremely disabling for many in our community. There are often limited treatment options, and many of the underlying causes are not known. My research aims to use new ways to analyse the human genome to identify genetic causes and understand how they lead to blindness.”

Robyn Jamieson
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, immortalization 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 protein, an important tumour suppressor, and how it functions to prevent cancers.”

Antony Braithwaite

Highlights

The Cell Transformation Unit published ten peer-reviewed papers in 2011. Some achievements include: developing a new technique for precisely measuring cell cycle distribution and DNA ploidy in tissue samples, allowing researchers to take a look in vivo at the effects of chemotherapeutic agents and other drugs; finding that p53 mutation was involved in the emergence of multi-drug resistant cancer cells; and determining the means by which PAX8 promotes tumour cell growth.

Continuing Research Areas

The Cell Transformation Unit, headed by Professor Antony Braithwaite, closed its doors in 2011 after Professor Braithwaite returned home to New Zealand. Some of the work carried out by this unit continues on at CMBR, however, with some former team members now working under the umbrella of the Cancer Research Unit, which continues to work closely with Professor Braithwaite and his group in Dunedin.

p53 isoforms

p53 is one of the most important tumour suppressing genes in human cells. Children born with defects in p53 suffer from multiple tumours from an early age. However we have discovered a particular variant (known as an isoform) of human p53 that does not act as a tumour suppressor but instead enhances tumour formation. We are investigating how this variant of p53 works to cause cancer as it may provide a useful target for novel cancer therapies. During our investigations into this p53 variant, we also discovered that this gene may be involved in autoimmunity.

Telomerase structure

Telomeres, the repetitive DNA-protein complexes at the ends of linear chromosomes, shorten with each cycle of DNA replication, providing a counting mechanism to limit the number of times a cell can divide. Most cancer cells have activated the enzyme telomerase to add telomeric DNA repeats and thereby counteract telomere shortening, allowing for unlimited proliferation. A majority (>85%) of all human cancers depend on telomerase for their growth. In contrast, normal cells have undetectable or very low levels of telomerase. Inhibition of telomerase is therefore a promising avenue for development of anti-cancer treatments that should be effective against a broad range of cancers while displaying few side effects. Our research aims to determine the high-resolution 3-D structure of telomerase, which will provide a foundation for rational drug design against this promising target.

Cell cycle arrest

The incidence of cancer varies significantly among the different tissues and organs of our body. More than 40% of newly diagnosed cancers arise from cells of the prostate, breast or bowel, while other organs, such as the heart, are very rarely affected. The molecular mechanisms underlying such tissue specificity are poorly understood. In order to develop novel strategies for the prevention of cancer, we aim to decipher the molecular basis of tumour suppression in different tissues. A current focus addresses the significance of one particular mechanism, cell cycle arrest, which is regarded as central for tumour suppression and the success of chemotherapy but has not been studied in different tissues in vivo before. In addition, we explore the tumour suppressor protein, p53, and have characterized a number of experimental anti-cancer drugs that target p53 and are now being tested in clinical trials.

Oncoprotein, YB-1

Understanding how YB-1 functions as an oncoprotein at a molecular level is central to a better understanding of its association with cancer. The posttranslational modification of YB-1 has not yet been characterised properly, nor is the mechanism behind its nuclear translocation understood. Both of these phenomena are thought to be behind YB-1’s oncogenicity, and its association with aggressive, drug-resistant tumours. We aim to uncover how YB-1 induces drug resistance, tumour aggressiveness, and poor patient outcome in a variety of cancers. We recently identified several novel phosphorylation sites of YB-1, which will give us some insight into its oncogenic properties.

The Embryology Unit is headed by Professor Patrick Tam, whose research focuses on the cellular and molecular mechanisms of body patterning during mouse development. Professor Tam’s research includes pioneering the application of micromanipulation and embryo culture for analysing mouse embryos and examining the development of the craniofacial structure and embryonic gut. The embryological analysis undertaken by his team at CMRI has enabled the construction of a series of fate-maps revealing the organisation of the basic body plan of the early embryo. This in-depth knowledge of cell differentiation during early embryogenesis laid the foundation for directing the differentiation of mouse stem cells into clinically useful cell types for therapy in regenerative medicine. His other current research is on the function of RNA binding protein and importin, a transporter of protein, in embryonic development.

“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.”

Patrick Tam

Highlights

The Embryology Unit published eight peer-reviewed scientific papers in 2011, two of these in the prestigious journal Development. Their efforts were also recognised externally with the awarding of two NHMRC Project grants and an ARC Discovery Project grant. Professor Tam achieved special recognition for his achievements when he was elected Fellow of the Royal Society of London.

Research Areas

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 the Lhx1 gene. Head abnormalities also occur in Saethre-Chotzen syndrome, caused by errors in the TWIST gene. We used mouse models to show that loss of twist affects different components of the craniofacial skeleton and the muscles of the face, eyes and jaws. Losing twist 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.

Developmental function of Importin, an importer of protein into the nucleus

Importin 13 is a member of a large importin & 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 tests-specific variant (“Tmph13”). Our analysis of Imp13 mutant mice
All 10 trillion cells in the human body start from a single cell.
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.

The CMRI Bioinformatics Unit is a newly established research, training and service facility dedicated to building bioinformatics and computational biology capability within CMRI. Under the leadership of Associate Professor Jonathan Arthur, the unit will:

- coordinate bioinformatics activity within CMRI
- provide a professional support and development network for bioinformatics staff embedded in CMRI research groups
- collaborate with CMRI research groups on research projects with bioinformatics components
- provide training and education for laboratory-based research staff and students to develop computational biology skills
- provide 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 will work collaboratively with other bioinformatics initiatives throughout NSW and Australia.
Genes code for proteins, the vital parts of living cells.

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™ Australia

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 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. Dr Amanda Capes-Davis was founding manager and helped establish CellBank Australia’s procedures; she continues to work as a consultant with CellBank Australia. As a member of ATCC’s Standard Development Organisation ASN-0002, Dr Capes-Davis contributed to the development of the international standard for authentication of human cell lines, released in 2012.

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. The Lady Mary Fairfax CellBank Australia 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 since July 2007.

The Biomedical Proteomics Facility at CMRI is a collaborative research resource that combines applied proteomics with the development of mass spectrometry (MS)-based qualitative and quantitative methods for protein identification and characterisation. The facility supports CMRI and the Westmead Research Hub, as well as collaborations with groups and individuals from around Australia and the world.

Proteomics is the ability to study proteins in our cells and tissues on a very large scale, rather than one at a time. The successful study of important cellular proteins depends largely on the experimental design and requires a great deal of careful planning. The facility aids biomedical research groups and individuals by offering access to equipment and methodology as well as expertise in the assessment of feasibility and strategy development for projects and programs involving MS and proteomics analysis.

In 2009-11, CMRI undertook a full refurbishment and extensive upgrade of the facility. Major funding, from the Cancer Institute NSW (CINSW), the Australian Research Council Linkage Infrastructure, Equipment and Facilities scheme (ARC LIEF), and the Ian Potter Foundation provided two MS systems for advanced phosphoproteomics research.

An additional four MS systems were purchased with generous funding from the Australian Cancer Research Foundation (ACRF) and the Ramaciotti Foundations to equip the new Australian Cancer Research Foundation Centre for Kinomics (ACRF-CK). Currently the facility houses a total of seven fully functional mass spectrometry systems providing a massive increase in capacity and capability.

What is Mass Spectrometry?

Mass Spectrometry (MS) is an extremely powerful analytical technique that underpins all modern day biomolecular science. It measures molecules to determine their weights, thus facilitating the identification and characterisation 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.

Example Proteomics Project: Dynamin

The question: is it possible to control nerve communication to ultimately treat various brain and nerve disorders?

Many years ago, the Cell Signalling Unit discovered that the protein dynamin plays a central role in a process called endocytosis, which is crucial to nerve communication (or nerve signalling). The group initially discovered dynamin as a phosphoprotein (a protein with a phosphate molecule attached to it) that is rapidly de-phosphorylated upon stimulation of nerve terminals. Using various techniques, including proteomics, the group deciphered the molecular mechanisms of dynamin’s phosphorylation cycle, and they have now identified all of the specific sites of phosphorylation in dynamin. Their work revealed that each site plays an essential role in endocytosis, and that they act cooperatively for maximal effect. They were also able to discover dynamin’s protein partner for endocytosis in neurons. These findings have led directly to the development of a new class of drugs to potentially treat epilepsy and to greater understanding of nerve communication that may one day lead to treatments for other nerve disorders.

The acquisition of new, cutting-edge equipment has resulted in an immediate surge in interest and demand for access, opening opportunities for exciting new collaborations.
What is Kinomics?

Kinomics is a subset of proteomics and is the study of all of the protein kinases expressed in a cell or tissue at any point in time. Kinases are proteins that act as “master switches” for many normal cell functions in the body and are the major new cancer drug targets of the 21st century. Kinases direct phosphorylation-based signalling inside cells. While the human genome encodes 518 protein kinase genes, approximately 200 of them are present in any one cell or tissue at any one time, making up the cellular “kinome”.

Kinomics is a completely new medical research discipline, based on identification of the cellular kinome in a rapid, systematic and global way. Combining chemical biology with MS has allowed development of new ways to identify and study the near complete cellular kinome in a single workflow. Kinomics research is a continuous pipeline, which requires two distinct classes of MS equipment: “discovery” instruments for identification and characterization of kinases; and “quantitative” systems for large scale kinase quantification, as well as verification, validation and profiling.

Comprehensive analysis of the kinome will improve our understanding of cell signalling and diseases where this signalling has gone awry, including cancer, neurological conditions, cardiovascular diseases, inflammatory conditions and asthma. Kinomics has enormous potential to help researchers identify therapeutically relevant protein kinase targets for accelerating drug discovery.

Collaborations have already been established with three universities, five medical research institutes, and a total of 23 medical research teams across NSW. In addition, cancer research teams throughout the nation will benefit from the ACRF-CFK, as all will have the opportunity to employ the Centre’s facilities for their projects.

Through the development of Kinomics technology and its collaborations with research teams across Australia, the Centre will enable 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.

UoN houses a flow chemistry laboratory, where they have developed KinoClick™ beads, a new tool for direct profiling of cellular protein kinases. CMRI houses a mass spectrometry (MS) laboratory to undertake initial evaluation and optimization of KinoClick beads, perform quality control and sample analysis for collaborating research teams.
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. More than half of the Institute’s revenue comes from private fundraising 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 2011 and acknowledge supporters who gave generously of their time and money to help create a healthier, brighter future for all children.

Q) How many wrong ‘letters’ are needed to result in a genetic disease?
A) One
Jeans for Genes is the major national fundraiser of Children’s Medical Research Institute. In 2011, more than two million Australians united in a stance against childhood disease and donned their favourite pair of jeans or donated to support CMRI’s vital research work. Over $4 million in revenue was achieved, taking the total raised since Jeans for Genes’ inception to approximately $60 million.

While awareness of the Jeans for Genes brand in the general public is high at 87%, one of the key opportunities is to create a stronger association between the cause and the campaign. The advertising campaign in 2011 asked the public to help ‘patch up our genes’ and support the scientists at CMRI. For the first time in the Institute’s history, the 2012 marketing campaign will promote CMRI as the direct recipient of Jeans for Genes fundraising. The 2012 campaign mobilises the enthusiasm and vibrancy of children and their “pester power” to link the cause to the campaign.

Jeans for Genes relies on loyal retail partners and businesses who sell campaign merchandise, including our double-helix badge, and help promote CMRI’s cause. Key retail partners for 2011 were Big W, Best & Less, Gloria Jean’s Coffee, Westpac, Jeanswest, Lovers, The Warehouse, Chicken Feed, Crazy Clarks and Go-Lo, Infocus Money Management, HCF, Factorie, Franklins, Harvey Norman, Domayne, Joyce Mayne, Newcastle Permanent Building Society, Outback Steakhouse, and Pharmacy Guild.

More than two thousand schools across Australia participated in the campaign. Students proudly wear their jeans to school to support our cause; many high school students also donate their time to help sell badges to the public.

The Jeans for Genes campaign culminates in the Gala Dinner at the end of August, featuring an auction of celebrity jeans transformed into works of art by Australian artists who donate their time and talent. 430 people attended the 2011 event which raised $180,000 from ticket sales, a raffle, live auction and donations on the night.

Jeans for Genes not only contributes essential funds for our research programs, it also raises the profile of the Institute and lets Australians know about the world-leading research being conducted at CMRI.

<table>
<thead>
<tr>
<th>Event/Location</th>
<th>Amount Raised</th>
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<tbody>
<tr>
<td>Canberra Committee</td>
<td>$70,000</td>
</tr>
<tr>
<td>2101 Schools participated in Jeans for Genes</td>
<td></td>
</tr>
<tr>
<td>The annual Earl Page Coast Run</td>
<td>$39,000</td>
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<tr>
<td>Gala Dinner and Art Auction</td>
<td>$180,000</td>
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<tr>
<td>Hills Committee Mother’s Day Luncheon</td>
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<td>The barristers appointed NSW Senior Counsel in 2011</td>
<td>$70,000</td>
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</tbody>
</table>
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 Hills Committee Mother’s Day Luncheon and the 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 2011, were:

- Canberra Committee’s Annual Luncheon
- Quirindi Committee’s Country Music Spectacular
- Gerringong Committee’s 21st Annual Quilt Show
- Bill Waugh Memorial Cup Tennis Day
- Melbourne Cup luncheons, sweeps and raffles held by Kangaroo Valley, Racquet and Northern beaches committees

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 would like to give special thanks to our major supporters, including the Rotary Club of Sydney, which donated $170,000 in 2011. Mr James Fairfax continues his generous support of our Embryology Research Unit, and there were also substantial donations from Mrs Joan M Barnet, Franklins, and J.J. Richards & Sons.

We also acknowledge the long term support of the Judith Hyam Memorial Trust Fund for Medical Research whose generosity has enabled the continuance of two named positions in our Cancer Research Unit. One of the young PhD students supported by Judith Hyam graduated in 2011 and plans to continue on doing cancer research.

Our corporate partners are important to our fundraising efforts, and we are fortunate to have long standing relationships with a number of companies. Kimberly-Clark continued their support of a named Research Fellowship (Kimberly-Clark Australia supporting Dr David Loebel in our Embryology Unit) and financially supported our Jeans for Genes campaign. 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, Allen & O’Haren, and AB Sciex for their generous support throughout 2011.

In the year ahead, we are determined to continue developing long term relationships with all our supporters and partners, including our newly formed community partnership with Sydney FC and our new retail partnership with Woolworths to sell our campaign merchandise in their stores nation-wide. We are very excited about the possibilities for 2012 and look forward to seeing what we can achieve together.

Bequests

One of the simplest things someone can do to help support CMRI is to leave a bequest in their will, it’s a lasting legacy that will benefit future generations of children. CMRI continues to receive generous bequests from a wide range of people, many who have been long term supporters of the organisation or have a personal connection to the cause. Bequests allow CMRI to plan for the future and support long term research projects.

CMRI Redevelopment Campaign

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.

With a greater number of scientists at the Institute, we can accelerate our research capacity in core areas and grow our international reputation. This is important in ensuring we retain leading Australian researchers, as well as attracting international talent.

To achieve our vision of growth, CMRI has plans to redevelop its building from its current two storeys to seven stores. Our proposed redevelopment is part of ongoing development plans for the whole Westmead research precinct, all of which will create a world-leading centre for research facilities. The precinct will be better able to pool resources, sharing access to cutting edge equipment and increasing the potential for inter-disciplinary collaboration.

CMRI recently received the $20m grant promised in last year’s state budget. As a result, the Board of CMRI has agreed to commence detailed design and construction plans. The first stage of this is a tower in our front courtyard that will increase our capacity by two thirds at a cost of $29m. We expect to complete this construction in 2014 and are seeking the balance of the funds from private and other government sources. A second stage will then commence, provided a further $36m of funding is committed.
Star Alliance

Star Alliance’s 26 members include some of the world’s leading airlines, such as Singapore Airlines, Air New Zealand and United. Star Alliance unveiled a Jeans for Genes travel incentive in mid 2011, which raised a total of $20,450. “The world’s leading airline network was honoured to be helping an Australian organisation undertaking world-class research,” said Star Alliance Country Steering Committee Chair, Alison Espley.

In addition to this valuable contribution to the Jeans for Genes campaign, Star Alliance continues to directly support CMRI. Each year, one of CMRI’s top PhD students is chosen to receive the Star Alliance Travel Scholarship, which provides a Round the World ticket for the winner to attend an international conference or visit laboratories overseas to enhance his/her knowledge and research skills. Allison Dane, winner of the 2011 Star Alliance scholarship, received the award from Star Alliance Business Manager, Brian Garside, at the annual Jeans for Genes Gala Dinner in Sydney.

Allison travelled to the European Society of Gene and Cell Therapy Meeting in Brighton UK to present her research findings. Also thanks to the Star Alliance Travel Scholarship, Allison was able to obtain a post-doctoral position in Milan, which will further her scientific training and enable her to acquire new skills that will benefit Australian science when she returns.

Allison says, “I am extremely grateful for the scholarship, which allowed me to discuss my research with leaders in the field and bring back ideas for new directions to take the work. I also made contacts that will help establish more collaborations in the future.”

The inaugural Star Alliance scholarship was presented in 2010 to Josh Stern, a PhD student in the Cell Biology Unit at CMRI, who says, “This kind of community support is a very powerful motivator. We’re doing this work to help children and the community. Knowing that the community cares and is involved in the process is extremely important.”

Corporate Partnership

All of the research programs at CMRI and in the Westmead Research Hub benefit from these shared resources, which include an Electron Microscope Laboratory and a Biomedical Proteomics Facility, the latter based CMRI, as well as several major pieces of equipment. 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 of a major Australian research centre.

The Westmead Research Hub is a coalition that includes CMRI, Westmead Hospital (WH), Children’s Hospital Westmead (CHW), and Westmead Millennium Institute (WMI). Scientists across the Westmead precinct collaborate, sharing knowledge and expertise, but the Hub also coordinates the purchase and sharing of major equipment.

Westmead Research Hub

The Westmead Research Hub is a coalition that includes CMRI, Westmead Hospital (WH), Children’s Hospital Westmead (CHW), and Westmead Millennium Institute (WMI). Scientists across the Westmead precinct collaborate, sharing knowledge and expertise, but the Hub also coordinates the purchase and sharing of major equipment.
All humans are 99.9% genetically identical to one another, no matter their race, except for identical twins, who are 100% identical.

GOVERNANCE AND FINANCE

CMRI is an independent research institute based in Westmead, NSW. The Institute employs approximately 150 people, including over 100 full-time scientists and PhD students, as well as operational and administrative support staff and a team of fundraisers. The organisational structure of CMRI reflects its corporate governance and areas of responsibility.
Board of Directors

Professor Frank Martin MBBS FRANZCO FRACS AM 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 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 National Museum of Australia, and is a member of the Institute’s Intellectual Property Committee and Finance & Investment Committee. He is also a member of the Intellectual Property Committee and chairs the Nomination and Remuneration Committee.

Mrs Carolyn Forster OAM Vice-President
Carolyn Forster has been a member of the Canberra Committee of CMRI since 1973, serving twice as President and twice as Treasurer. She has worked in the Federal Parliament for 11 years, in the Senate, the House of Representatives, and the Ministry. She has 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 President of the Friends of the National Museum of Australia, and Vice President Africa, Asia, Pacific of the World Federation of Friends of Museums. She is Chair of the Church of St. Andrew Conservation and Restoration Foundation and serves on a number of other committees. She received an ACT Women’s Award in 1996, a Centenary Medal in 2003, and an Order of Australia Medal 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 Nomination & Remuneration Committee.

Mr Rodney Atfield FIA FIAA FAIL 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 a former President and Life Member of the Institute of Actuaries of Australia. 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 Avant Insurance Limited, Hannover Life Re and ING 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 & Risk Committee and Finance & Investment Committee. He is also a member of the Intellectual Property Committee and the Nominations & Remuneration Committee.

Mr John Dunlop AM
John Dunlop was a member of the Management Committee of CMRI from 1973 to 1985, serving as President from 1983 to 1985. As an inaugural member of the Board of the Institute, he served as Honorary Treasurer from 1985 to 1991. He is a Chairman of the Hospitals Contribution Fund of Australia Limited and an independent member of a number of governance committees of The Children’s Hospital at Westmead. He was President of The Children’s Hospital at Westmead from 1983 to 2007, Managing Director of Edwards Dunlop and Company Limited between 1978 and 1989, and Director of Health Super Pty Ltd between 2000 and 2007.

Mrs Kathryn North AM MD BSc (Med) PhD FRACP
Professor Kathryn North is Head of the Institute for Neuroscience and Mental Health, and Associate Dean of the School of Medicine at Monash University. Prior to this appointment she was Professor of Paediatrics and Child Health and Head of the Division of Paediatrics and Child Health, Faculty of Medicine, University of Sydney. Following a Postdoctoral Fellowship in Boston, she returned to Australia in 1995 as the recipient of the Children’s Hospital Research Career Development Award. Her research interests focus on inherited childhood muscle disorders and neurofibromatosis. In 2000, she received the Sandler Award for achievement in neuromuscular research and in 2008 was honoured by the Human Genetics Society of Australasia for her achievements in genetic research and as visiting Professor to the Harvard Genetics Program. She received the GSK Award for Research Excellence in 2011 and became a Member of the Order of Australia in January 2012. Professor North is past Chairman of the Children’s Hospital Research Laboratories Committee and an Executive Board member of the World Muscle Society. She is currently a member of the Children’s Hospital Research Executive and Research Committee, a member of the University of Sydney Medical Deans Advisory Committee, and Chairman of the Genetics Sub Committee of the Australian Association of Neurologists. She joined the Board of CMRI in 2000.
Board of Directors continued

Mrs Patti Payne OAM MPS PhD
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 in 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 deeply 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. A fifth died in infancy from a genetically related condition. She was awarded the Medal of the Order of Australia in 2006. Mrs Payne was elected to the Board in October 2000.

Professor Kathryn North

Professor Roger Reddel BSc (Med) MBBS PhD FRACP FRCPA
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 his 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 a Cancer Council NSW’s Bicentennial Fellowship. In 2007, Professor Reddel was awarded the Ramaciotti Medal for Excellence in Biomedical Research, and in 2010 was elected as a Fellow of the Australian Academy of Science. He received the Premier’s Award for Outstanding Cancer Researcher of the Year in 2011. He 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 (CCAF). Professor Reddel has been Director of the Institute since 2007 and serves on the Institute’s Finance & Investment Committee.

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 Clancy 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.

Hon. Craig Knowles

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; Member of the Advisory Committee, Urban Research Centre, University of Western Sydney; President, Asthma Foundation, NSW; Trustee of the Hoc Mai Foundation; Director, Black Dog Institute; Advisor, Investec Bank (Australia) Ltd; Director, Tulich Family Communities Aged Care; Independent Chairman, Prospect Water Partnership; Independent Chairman, Aj Jennings Property Fund; 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) and Minister for Forests and Minister for Lands (2003–January 2005). Mr Knowles is a Fellow of the Australian Property Institute and a Certified Practising Valuer. He joined the CMRI Board in May 2007.

Meet a Volunteer

Denva Barber
Denva Barber first visited CMRI in February 1997 as part of a Discovery Day tour. “I thought it would be a marvellous place to work,” she says. “I was impressed by the credible financial management of CMRI as well as the spirit of communication among the scientists and their willingness to share research internationally.”

Denva signed on to assist CMRI’s Community Relations Manager, Jennifer Philips, and has been volunteering her time for the last 15 years.

“I enjoy the company of the people here and the surprises each day brings. I’m doing things I’ve never done before, such as making ‘thank you’ calls, doing mailings, even doing this interview!”

Denva also served for three years on the CMRI Animal Care and Ethics Committee as a representative of the public. “It was something I never expected to do, but when asked I said yes, and I enjoyed it very much. I learned more about what CMRI is doing by reading the scientists’ reports.”

Always a hard worker, Denva spent 40 years in various roles for the Service and Electricity Commission and then worked in the canteen of Canterbury Hospital before it was pulled down. When asked how much longer she plans to continue volunteering at CMRI, she says,

“I will keep going until I can’t.”

Denva Barber
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:

- Professor Frank Martin
- Mrs Carolyn Forster
- Mr Rod Atfield (Chair)
- Mr John Bevins

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:

- Professor Frank Martin (Chair)
- Mrs Carolyn Forster
- Mr Rod Atfield

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

- Professor Frank Martin
- Mrs Carolyn Forster
- Mr Rod Atfield (Chair)
- Mr John Bevins
- Mr Paul Scully
- Dr Don Stammer
- Prof. Roger Reddel
- Mr Ralph Mitchell

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

Director

Intellectual Property Committee

Audit & Risk Committee

Finance & Investment Committee

Nominations & Remuneration Committee

Operations
- Lab Management
- Bio Services
- Building Facilities
- Information & Communications Technology

Research
- Cancer Research
- Cell Biology
- Cell Cycle
- Embryology
- Gene Therapy
- Cell Signalling
- Cell Transformation

Specialised Facilities
- CellBank Australia™
- Bioinformatics
- Biomedical Proteomics Facility
- (including ACRF Centre for Kinomics™)

Executive
- Director’s Office
- Finance
- Human Resources
- Commercialisation & Affiliations
- Marketing & Communications
- Supporter Services

Fundraising
- 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

Advisory Committees

Scientific Advisory Centre for Kinomics™

Scientific Advisory CellBank Australia™

Cancer Consumer Panel

Fundraising
CMRI continued to weather the financial impacts of the Australian and global economies in 2011. Despite challenges in investment markets and natural disasters impacting on philanthropic giving patterns, the Institute maintained its level of expenditure on its research activities. The Institute manages its activities and finances to allow it to maintain and potentially grow its research in the foreseeable future. To this end, net surpluses generated over previous periods help the Institute to operate consistently during economic downturns.

Our researchers continue to compete successfully for public funding through grant applications to government agencies such as the National Health and Medical Research Council and the Cancer Institute of New South Wales. In addition, our researchers apply for funds from a variety of private trusts and foundations, undergoing rigorous peer reviews as well as assisting fundraising teams with more community-minded requests. Grant income is used to fund research staff costs and consumables required for projects. In addition, certain grants are awarded for the acquisition of highly specialised equipment and services, allowing CMRI to stay at the forefront of its areas of expertise. Slightly over one third of our income was generated by research grant success in 2011.

A similar amount of money is generated from our fundraising team’s efforts. Fundraising is conducted directly in the name of CMRI, for example direct mail appeals to our network of supporters, and activities and events conducted by our dedicated Community Committees. Some of our supporters and committee members have been working on CMRI’s behalf for 50 years or more.

In addition to fundraising for CMRI, we created and developed the national brand ‘Jeans for Genes’, which fundraises in every state, particularly the annual Jeans for Genes Day in August. The Institute is very conscious of sometimes publicised rates of fundraising expenses to fundraising revenue and strives to maximise returns against the costs it incurs. In 2011, this ratio was 36%.

The third major source of income for the Institute is investment income, which comprised just under one third of income in 2011. Over many years, and based on its fundraising activities, CMRI has built up an Investment Fund which is allocated across a selection of growth and defensive assets, thereby balancing risk and returns. Using professional investment managers and advisers, an Investment sub-committee of the Board of CMRI oversees investment decisions and activities. In 2011, returns improved from depressed previous periods; however, markets remain volatile and performance can fluctuate. Although not a significant income stream at present, the Institute is looking for opportunities to exploit its intellectual property through commercial arrangements. Various research-based patents and trademarks are held and are being supported annually. In 2011, international sales of certain products under licensing arrangement commenced and will continue to grow in 2012 and beyond. The Institute also operates CellBank Australia, which generates commercial sales, albeit on a cost recovery formula. Combined proceeds from these commercialisation activities were approximately half a million dollars in 2011, which were reinvested in our research programs.

Ralph Mitchell
Chief Financial Officer
May 2012
Sources of Revenue and Expenditures

For 12 months ended 31 December 2011

Total – $20 million

Revenue

- Fundraising: 34%
- Investment Income: 11%
- Research Grant Income: 28%

Expenditure

- Fundraising: 19%
- Administration and Facilities: 70%
- Research: 11%

For 6 months ended 31 December 2010

Total – $14 million

Revenue

- Fundraising: 38%
- Investment Income: 20%
- Research Grant Income: 28%

Expenditure

- Fundraising: 42%
- Administration and Facilities: 64%
- Research: 15%

Financial Summary

Profit and Loss Statement

<table>
<thead>
<tr>
<th></th>
<th>12-months Dec 2011</th>
<th>6-months Dec 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revenues</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research</td>
<td>7,460</td>
<td>5,921</td>
</tr>
<tr>
<td>Fundraising</td>
<td>6,659</td>
<td>5,429</td>
</tr>
<tr>
<td>Investments</td>
<td>5,385</td>
<td>2,834</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>19,504</td>
<td>14,184</td>
</tr>
</tbody>
</table>

| **Expenses**         |                    |                   |
| Research             | 15,461             | 8,144             |
| Fundraising          | 2,423              | 1,956             |
| Administration and facilities | 4,308 | 2,690 |
| **Total**            | 22,192             | 12,790            |

<table>
<thead>
<tr>
<th><strong>Surplus/(loss) before investment transactions</strong></th>
<th>12-months</th>
<th>6-months</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2,688)</td>
<td>1,394</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Surplus/(loss) from continuing operations</strong></th>
<th>12-months</th>
<th>6-months</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2,487)</td>
<td>1,435</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Other comprehensive income from Available-for-sale financial assets</strong></th>
<th>12-months</th>
<th>6-months</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2,630)</td>
<td>342</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Total comprehensive income/(loss) for the period</strong></th>
<th>12-months</th>
<th>6-months</th>
</tr>
</thead>
<tbody>
<tr>
<td>(5,117)</td>
<td>1,778</td>
<td></td>
</tr>
</tbody>
</table>

Balance Sheet

<table>
<thead>
<tr>
<th></th>
<th>As at: 31 Dec 2011</th>
<th>As at: 31 Dec 2010</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>9,695</td>
<td>8,598</td>
</tr>
<tr>
<td>Other Financial Assets</td>
<td>60,901</td>
<td>66,465</td>
</tr>
<tr>
<td>Property, Plant and Equipment</td>
<td>14,959</td>
<td>15,223</td>
</tr>
<tr>
<td>Other Non-current Assets</td>
<td>1,238</td>
<td>1,101</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>86,794</td>
<td>91,387</td>
</tr>
</tbody>
</table>

| **Liabilities**      |                    |                    |
| Current Liabilities  | 4,384              | 3,863              |
| Non-current Liabilities | 262              | 259               |
| **Total**            | 4,645              | 4,122              |

| **Net Assets**       | 82,149             | 87,265             |

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/Annual Reports.
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.

Thank you.