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About CMRI

Children’s Medical Research Institute (CMRI) was established in 1958 by members of the Australian community who came together saying “we need to do something for the children.” At that time, the causes of many childhood illnesses, birth defects and genetic diseases were unknown. The structure of DNA—the set of instructions found in every living thing, dictating whether it will be human, plant or animal, healthy or ill—had only been discovered a few years before. It was a time of tremendous uncertainty but also of tremendous potential. CMRI was created to seize that potential.

With the support of the community, CMRI began the long and difficult work of making tomorrow better. We found collaborators and colleagues around the world with the same goals and, together, have made tremendous strides in transforming the ‘unknown’ into the ‘known’.

CMRI developed microsurgery techniques for infants and small children, improved the survival of premature babies, raised awareness of the dangers of alcohol during pregnancy, and introduced vaccines so that many birth defects and serious childhood illnesses, which could be fatal, are now simply prevented. All of these things are now taken for granted as part of routine healthcare.

Today we are going after even more challenging goals. One of these is to find treatments for every type of cancer. Every type. We are developing drug treatments for epilepsy using a totally new principle of action that could help the 1 in 3 epileptics who don’t respond to current medications. Our gene therapy work is the most advanced in Australia, with several clinical trials underway, and has the potential to cure previously incurable inherited diseases in children.

We are a small institute with very big goals—so we can’t stay small. CMRI is undergoing its first major expansion in 20 years, which will help us to reach these goals faster. And we’re celebrating!

In these pages you will learn about our recent achievements, but you will also learn more about the Institute’s vision, our successes over the past 20 years, and our plans for the next twenty.

Welcome to our annual report for the calendar year, January through December, 2012.
CMRI is celebrating 20 years at Westmead

What we’ve accomplished in the last 20 years:

• Found a single genetic defect can cause cleft lip and palate
• Fate map of the early embryo to help us understand many developmental problems
• Identification of the components of telomerase, which will be important for treating 85% of all cancers
• Discovery of the Alternative Lengthening of Telomeres (ALT) mechanism, which will lead to treatments for the other 15% of cancers
• Developing a blood test for ALT cancers that will allow physicians to diagnose and plan treatments for cancers such as aggressive glioblastoma brain tumours
• Partnering with the Children’s Hospital Westmead on a cure for genetic liver disease, with clinical trials about to begin
• Discovering and developing a new class of drugs for treating epilepsy

What we plan to accomplish in the next 20 years:

• Develop epilepsy treatments that will help children (and adults) around the world
• Develop new treatments for kidney disease and diabetes
• Gene therapy cures for rare genetic diseases in children
• New treatments for infectious diseases
• Telomere research to help us understand predisposition to disease
• Find new and better treatments for every type of cancer
Report from the President

“...This much-needed expansion will speed up our research endeavours by providing space for twelve additional laboratories and better infrastructure for our shared facilities.”

President: Frank Martin

Children’s Medical Research Institute is building for the future and in January 2013 began constructing the first stage of a planned five-stage redevelopment. This much-needed expansion will speed up our research endeavours by providing space for 12 additional laboratories and better infrastructure for our shared research facilities, including Bioinformatics and Biomedical Proteomics.

CMRI has continued to increase its scientific output and announced many important discoveries and developments in the areas of cancer, birth defects, gene therapy, epilepsy and neurobiology, with over 45 peer-reviewed publications released in 2012. The key findings from each research unit over the last year are set out in this annual report and its addendum.

I would like to draw particular attention to the official opening of the ACRF Centre for Kinomics at CMRI in September. This achievement could not have been possible without the hard work and original ideas of the researchers behind it. I congratulate Professor Phil Robinson of CMRI and Professor Adam McQuisbery of the University of Newcastle. Professors Robinson and McQuisbery have worked closely together for many years to create this revolutionary new Centre for Kinomics, whose goal is the development of improved therapies for conditions such as cancer and epilepsy.

We have had a very productive partnership with the University of Newcastle for more than a decade, and we were delighted that Professor Bill Hogarth (Pro Vice Chancellor) and Professor Mike Calford (Deputy Vice Chancellor, Research) were able to be present at the opening of this joint centre. CMRI is also grateful for the support of the Ian Potter and Ramaciotti Foundations and, especially, the Australian Cancer Research Foundation, who have lent their name to the facility, and all of whom have contributed funds towards the purchase of cutting edge mass spectrometry equipment underpinning this new field of research.

CMRI held a “Turning of the Sod” celebration on 12 November, 2012. This was a special date, marking the 20th anniversary of our building at Westmead and celebrating the imminent commencement of construction. Also celebrating 20 years is our Jeans for Genes fundraising campaign. Despite an ongoing economic downturn and a large increase in fundraising activity for a wide variety of causes, Jeans for Genes continues to attract loyal supporters and to contribute to our revenue streams.

The Australian public’s support is vital for funding our research, and especially the expanded programs that will be made possible by the building redevelopment. A restructuring of our Fundraising department was completed in 2012, which will help to minimise costs and increase income in 2013. An independent advisory firm was contracted to carry out a review of our expansion plans, including fundraising and research, and their analyses overwhelmingly support the benefits to the community of growing CMRI and the feasibility of our vision.

Finally, I would like to thank all of the people who are working hard for our success. Our Board Members continue to volunteer their time, expertise and energy. CMRI’s outstanding record of scientific achievement comes from the commitment of the scientists and research students whose work is laying the basis for more effective treatment of childhood diseases, and I thank them for their ongoing efforts. I also thank the administrative, fundraising, and operations staff of CMRI who make this possible. And, as always, a very special thank you to CMRI’s loyal and committed fundraising committees and the other volunteers who help us in so many ways.

Welcome to CMRI’s annual report for 2012.

Frank Martin
President
May 2013
Report from the Director

“CMRI’s strategy is to continue building on our existing research strengths, providing a concentration of scientists with complementary skills and ideas working together to solve problems that have previously been too tough to tackle.”

Director: Roger Reddel

Until twenty years ago, CMRI was located at Camperdown within the grounds of the Children’s Hospital, a site that had served the Institute well for over thirty years, but we were entering a new era of molecular research that required more advanced facilities and purpose-built laboratory space. So we constructed a new building at Westmead, next to the site of the New Children’s Hospital.

Now we find ourselves in a similar situation. To increase the rate at which discoveries by our researchers make their way into the clinic, we have a pressing need to expand all of our research programs. We also have an urgent need for a Bioinformatics facility to deal with the massive amounts of information generated by new sequencing and mass spectrometry technologies. CMRI operates two national facilities to benefit research across Australia — the ACRF Centre for Kinomics and CellBank Australia — and both are currently constrained by lack of space. So we have planned a five-stage redevelopment of our building that will house the purpose-built laboratories and facilities needed for the research that will benefit the next generation of children.

In the meantime, CMRI is continuing to do first-rate research. For example, in 2012, Annie Quan and Prof Phil Robinson of our Cell Signalling Unit identified a specific site in the Syndapin I protein that controls neuron outgrowth, a discovery which provides a better understanding of brain development. In the Cell Biology Unit, PhD student Josh Stern and Associate Professor Tracy Bryan gained a new understanding of how the telomerase enzyme is recruited to the ends of chromosomes, a process that will be important for finding new therapeutic targets with the potential to treat 85% of all cancers. And researchers from the Cancer Research and Embryology Units together made the discovery that the ALT mechanism is active at low levels in normal cells, which is important for understanding how ALT works and one day developing new treatments for the other 15% of all cancers.

CMRI’s strategy is to continue building on our existing research strengths, providing a concentration of scientists with complementary skills and ideas working together to solve problems that have previously been too tough to tackle. In 2012, two new research groups were formed, one headed by Dr Mark Graham within the Cell Signalling Unit and another by Dr Hilda Pickett in the Cancer Research Unit. Collaboration is critically important to the success of medical research. We have a strong relationship with the Children’s Hospital at Westmead, including a joint Gene Therapy Unit, which has steadily become more and more successful since it was first established 17 years ago; it now has several clinical trials underway. CMRI is a founding member of the Kids Cancer Alliance, an initiative that encompasses almost all of the paediatric cancer doctors and researchers throughout NSW, focussing their joint efforts to ensure that children with cancer benefit from research discoveries as quickly as possible.

CMRI is also a founding member of the Westmead Research Hub, a collective of collaborating research institutions that share equipment and expertise to maximise the value of donated money (see page 44). Westmead is already the largest healthcare and medical research precinct in the nation, and we are strongly supporting plans for healthcare professionals, educators and researchers to integrate their efforts for the benefit of all.

On 12 November, 2012 we celebrated our 20 years at Westmead, and on this date we also ‘turned the sod’ for the first stage of our redevelopment, made possible thanks to a $20 million contribution from the NSW State Government. The event was attended by almost two hundred people, a sampling of all those who make CMRI’s work possible: our committee members, researchers and other staff, Board, supporters, colleagues, and friends. Political support was shown by both parties, Federal and State, with Minister Jillian Skinner, Senator Marise Payne, Julie Owens MP and Geoff Lee MP all in attendance - all spoke eloquently about the benefits of investing in medical research and about the work of CMRI.

This issue of the annual report will highlight our research achievements over the last two decades and our goals for the years ahead. Westmead is where we are based geographically, but our discoveries have no boundaries and have the potential to benefit children and their families everywhere. Please join us as we celebrate our expanding research capacity and what it means for creating a future where an increasing number of childhood diseases become things of the past.

Roger Reddel
Lorimer Dods Professor and Director
May 2013
Not all research is the same

CMRI conducts fundamental (meaning fundamentally important) medical and biological research. We ask the difficult questions. What causes cancer? How do we stop it? Why does development go wrong and how can we prevent it? How does the brain work? Can what we’ve learned about brain cells be put to use to treat epilepsy and other neurological disorders?
How can we make the future better?

CMRI scientists ask the difficult questions so they can get the important answers. This knowledge gives us the necessary tools to build a better future and enables us to help light the spark that will lead to tomorrow’s discoveries.
CMRI's Collaborations

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

Australia and New Zealand
- Baker IDI Heart and Diabetes Institute, Melbourne VIC
- Biomolecular Frontiers CoRE & ARC Centre of Excellence in Bioinformatics, Macquarie University, Sydney NSW
- Calvary Mater, Newcastle NSW
- Centenary Institute, University of Sydney NSW
- Children’s Cancer Institute Australia, Kensington NSW
- Clinical Geneticists & Ophthalmologists throughout Australia and New Zealand
- CSIRO Division of Health Sciences and Nutrition, Parkville VIC
- CSIRO Materials Science & Engineering, Parkville VIC
- Diamantina Institute, Centre for Immunology and Cancer Research, University of Queensland, Brisbane QLD
- Dunedin School of Medicine, University of Otago, New Zealand
- Institute for Molecular Biosciences, University of Queensland, Brisbane QLD
- John Hunter Hospital, Newcastle NSW
- Kids Research Institute, Westmead NSW
- Kolling Institute of Medical Research, St Leonards NSW
- Ludwig Institute for Cancer Research, Melbourne VIC
- Massey University, New Zealand
- Mental Health Research Institute, Parkville VIC
- Monash University, Melbourne VIC
- Murdoch Children’s Research Institute, Melbourne VIC
- Northern Cancer Institute (HRW), North Shore Private Hospital, St Leonards NSW
- Peter MacCallum Cancer Centre, East Melbourne VIC
- Queensland Brain Institute, Brisbane, QLD
- Queensland Institute of Medical Research, Herston QLD

- Royal North Shore Hospital, St Leonards NSW
- Save Sight Institute, University of Sydney, Sydney NSW
- School of Medical and Molecular Biosciences, University of Technology, Sydney NSW
- St Vincent’s Institute of Medical Research, Melbourne VIC
- Sydney Adventist Hospital, Wahroonga NSW
- The Children’s Hospital at Westmead, Westmead NSW
- The Royal Melbourne Hospital, Parkville VIC
- University of Auckland, New Zealand
- University of Melbourne, Parkville VIC
- University of New South Wales, Sydney NSW
- University of Newcastle, Newcastle NSW
- University of Otago, Dunedin, New Zealand
- University of Queensland, Brisbane QLD
- University of Sydney, Sydney NSW
- University of Wollongong, Wollongong NSW
- Victor Chang Cardiac Research Institute, Darlinghurst NSW
- Walter and Eliza Hall Institute, Melbourne VIC
- Westmead Millennium Institute, Westmead NSW
Europe

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

North America

- Albert Einstein Medical Centre, Philadelphia PA, USA
- Capital Biosciences Incorporated, USA
- Harvard Medical School, Boston, MA USA
- Institute of Cancer Genetics, Columbia University College of Physicians and Surgeons, New York NY, USA
- Massachusetts General Hospital, Boston MA, USA
- MD Anderson Cancer Center, University of Texas, Houston TX, USA
- National Institute of Allergy and Infectious Diseases (NIAID), Bethesda MD, USA
- National Institute of Child Health and Development, National Institutes of Health, Bethesda MD, USA
- Terry Fox Laboratory, BC Cancer Agency, Vancouver BC, Canada
- University of Massachusetts, USA
- University of Washington, Seattle WA, USA
- Wake Forest University, Wake Forest NC, USA
Established 1988

Unit Head: Professor Roger Reddel  
BSc (Med) MBBS PhD FRACP FAA,  
Lorimer Dods Professor and Director CMRI

What They Do

Trailblazing work on telomeres, which are important for senescence (aging) and all cancers. Main emphasis is on understanding the Alternative Lengthening of Telomeres (ALT) mechanism so they can develop treatments against ALT cancers, which are some of the most aggressive types.

Major Achievements:

1988  Cancer Research Unit forms at CMRI. Goal to understand cancer cell immortalisation in sufficient detail to find new cancer therapies

1995  Discovers Alternative Lengthening of Telomeres (ALT) mechanism of telomere maintenance in cancer. Creates an entirely new field of research

1999  Find diagnostic marker for ALT, called APBs. Also show that unknown factors in normal cells can repress ALT cancers.

2000  Demonstrate that ALT involves DNA recombination. First in the world to show this underlying mechanism

2007  First in world to identify composition of active telomerase enzyme complex in human cells

2009  Develop C-circle assay for measuring ALT activity in cancer. Discover telomere trimming mechanism that could one day be exploited to target and kill cancer cells

2011  C-circle assay is licensed for research use as a test for ALT cancers. Also determine the number of ‘frayed’ telomere ends needed to signal senescence or cell aging

2012  Involved in international Starr Consortium study identifying key genetic change (loss of ATRX) in ALT

2013  Demonstrate that ALT has a normal counterpart in cells and develop a new model system for studying the ALT mechanism

What’s Next

Extend utility of C-circle assay for diagnostic use and to screen for ALT inhibitors. Study key ALT proteins to reveal potential therapeutic drug targets.
“I trained as a medical oncologist and treated cancer patients every day, and so I saw firsthand the need for new treatments. It seemed self-evident that these would only come about through research, and I was very fortunate to be offered a great opportunity to be trained in laboratory research.

My goal from the start was to develop better therapeutics for cancer, and I set about studying immortalisation. Cancer cells are immortal (ie. able to grow forever) while the normal cells in our bodies are mortal. I expected that a new treatment that targeted immortality would have fewer side effects and be based on a more targeted principle than most previous treatments.

Despite this very focused goal, I have found over the years that research works best when there’s also curiosity and the love of science driving it. Elizabeth Blackburn won the Nobel Prize in 2009 for her discovery of telomerase in one-celled organisms, and she had nothing in mind when she made the discovery other than curiosity. Her discovery underpins many aspects of my work and is helping me and other researchers around the world look for new cancer treatments. Similarly, the invention of the C-circle assay by Jeremy Henson in my lab was the result of curiosity that initially had no translational goal in mind, but it has turned out to provide the first blood test for ALT cancers and will be instrumental in developing new treatments for aggressive tumours, such as glioblastomas.

Focused, translational-oriented research is needed to advance these discoveries to the next stages, where they can be useful to patients, and that’s where we are right now. However, we also need basic, curiosity-driven research to continue if we are to make the truly great discoveries. CMRI’s culture has long been supportive of both types of research (basic and translational), which underpins the success of our research programs.”

Professor Roger Reddel
Established late 2001

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

What They Do

The Cell Biology Unit focuses on one of the major factors in 85% of all cancers—telomerase. They study this protein in intricate detail so they can develop better cancer treatments with fewer side effects.

Major Achievements:

1995  Tracy Bryan discovers ALT mechanism of telomere maintenance, used by 15% of cancers
1997  Tracy Bryan trains in biochemistry under Nobel Laureate, Tom Cech at the University of Colorado, USA
2001  Cell Biology Unit formed at CMRI after Tracy Bryan returns from USA
2002  Develops assays to study human telomerase, important for 85% of all cancers
2006  Discovered that telomerase can extend a form of structured DNA, known as a G-quadruplex
2010  Developed assay to study recruitment of RNA component of telomerase to telomeres (necessary for 2012 finding to occur)
2009  Experiments to increase telomerase production for X-ray crystallography work
2012  Identified role of TEN domain in telomerase, an important anti-cancer drug target
2012  Found key proteins required for bringing telomerase to telomeres inside cells, thus revealing potential new anti-cancer drug targets. Collaboration with medicinal chemists to test G-quadruplex binding molecules as potential cancer treatments.

What’s Next

Pre-clinical trials of G-quadruplex binding molecules for cancer. X-ray crystallography studies of telomerase for targeted therapeutic drug development.
My research career began as a PhD student in Roger Reddel’s laboratory at CMRI. Scientists in the US had recently shown that human cancer cells, but not normal cells, had telomerase, an enzyme that allows the cancers to lengthen the DNA at the ends of their chromosomes (telomeres) and keep growing indefinitely (i.e., it is how the cancers became immortal). I travelled to Texas in the US to learn from researchers there and brought the technique for detecting telomerase back to Australia.

I started testing the extensive collection of cell lines Roger Reddel had gathered or created for his immortalisation work, and I kept finding cancer cells without telomerase. I thought I was doing something wrong and was told by my US colleagues that it simply meant the cells weren’t immortal (i.e., they were likely benign and not cancerous). I couldn’t dismiss my findings so easily, so I kept working and demonstrated that the cells were immortal and they definitely didn’t have telomerase activity. This was the discovery of the Alternative Lengthening of Telomeres mechanism (ALT). It has opened up a whole new field of cancer research and scientists all over the world are working on it now.

Despite being the discoverer of ALT, I chose to pursue my interest in telomerase instead, because as well as being present in about 85% of cancers, telomerase is also a fascinating molecule to study. I went back to the US for post-doctoral studies in order to learn new skills in biochemistry from Nobel Prize winner, Tom Cech. Once again, I came back to Australia bearing new knowledge to share with my colleagues here, and I opened up a new research unit at CMRI.

The techniques I learned from the Cech lab to study telomerase were based on single-celled organisms found in ponds, called Tetrahymena. They were what Elizabeth Blackburn used for her Nobel Prize-winning discovery of telomerase. My goal was to develop these techniques to study human telomerase so we could find ways to combat human cancers. The early years after setting up my lab at CMRI were devoted to building these methods.

My lab has also spent years studying strange DNA structures that can form in telomeres, called G-quadruplexes. There is a lot of excitement around the world now about the possibility of using drug treatments targeted to G-quadruplexes to treat cancer, and I’m currently collaborating with chemists at the University of Wollongong to test these treatments against cancer cells in the laboratory.

I’m also working in collaboration with my spouse, Dr Scott Cohen here at CMRI, as well as colleagues at St Vincent’s Institute and the CSIRO in Melbourne to discover the detailed structure of human telomerase. This is done using X-ray crystallography, a time-consuming technique that requires large amounts of telomerase protein, which is difficult to produce. There are no guarantees that we will succeed, but if we do, the benefits could be enormous. A ‘crystal structure’ of telomerase would allow us to intelligently design new anti-cancer drugs with pinpoint accuracy. It could revolutionize the search for new cancer treatments.

My approach to science is to pay attention to the details while not losing sight of the end-goal, and above all to not ignore surprising results. That’s how discoveries are made.”

Associate Professor Tracy Bryan
Established June 2011

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

What They Do

Study normal cell division in order to understand what makes cancer cells grow out of control. They also develop new anti-cancer treatments aimed at stopping cell division, especially in difficult to treat brain tumours.

Major Achievements:

2005 Megan Chircop publishes research paper establishing her in the cell cycle field
2006 Megan Chircop assumes position in Cell Signalling Unit at CMRI
2010 Show proof of concept for dynamin inhibitors in cell cycle and cancer therapy
2011 Cell Cycle Unit formed at CMRI. Two key basic research papers published on the topic of cytokinesis
2012 Lead compounds for cancer treatment successful, reducing brain tumour volume by 75%

What’s Next

If new compounds under production are suitable for use in humans, clinical trials may be only 3 years away.
“I began as a basic scientist interested in a fundamental understanding of the role of the cell cycle in cancer, specifically mitosis (the stage of the cell cycle where cells divide in order to reproduce), which is an underdeveloped field of study in Australia.

When I came to work for Prof Phil Robinson as a Group Leader in the Cell Signalling Unit at CMRI, Phil and Adam McCluskey (a medicinal chemist at the University of Newcastle), had developed small molecule inhibitors of the dynamin protein, a protein which I found was required for mitosis. Most new drugs in pre-clinical and clinical trials target mitosis, so investigating Phil and Adam’s compounds fitted with my interests and naturally led to developing these drugs for cancer therapy.

I believe that a translational research program needs continuing input from basic research in order to be successful. From our understanding of dynamin, I knew that the dynamin-inhibitory drugs I was testing should have an effect on brain tumours in mouse models. But nothing happened.

Fortunately, because I was certain of the basic research, my team used the mass spectrometry facilities at CMRI to look at how much drug was actually reaching the important tissues within the mice. There wasn’t enough where it needed to be, so we simply doubled the dose and saw an 80% reduction in tumour volume.

These lead compounds are now the basis for my current work, and they would have been overlooked in a standard drug discovery program. Ongoing basic research in parallel with translational programs helps keep us from going down the wrong roads.

My basic research is currently focused on learning more about the cell cycle in cancer, and this can inform future translational work. My team has identified several mitotic genes that are possible new drug targets. We also have a sub-program looking at centrosomes, which are a central scaffold for mitotic regulatory proteins.

All of this research will ultimately help us understand how cells divide and in turn act as the foundation for future work on developing cancer therapies.”

Dr Megan Chircop
Established 1996

Unit Head:
Professor Phillip Robinson
BSc (Hons) PhD, NHMRC Senior Principal Research Fellow

What They Do

The Cell Signalling Unit studies the detailed molecular mechanisms of how signals are sent from one cell to another in the body, with a focus on nerve cell signalling and developing new treatments for epilepsy and other neurological disorders, as well as using their understanding of dynamin and other signalling molecules to develop new treatments for a range of diseases.

Major Achievements:

1993 – Publications establish Phil Robinson as a world leader in the field of dynamin research and nerve cell signalling
1994 – Cell Signalling Unit established
2000 – Establish collaboration with medicinal chemist, Adam McCluskey
2003 – Identify the signalling that controls dynamin in neurons
2004 – First to report an inhibitor of dynamin and endocytosis
2006 – First to show that dynamin-dependent endocytosis controls nerve transmission
2010 – Reveal further complexity in the signalling that controls dynamin and find that dynamin regulates long term nerve transmission changes. With Megan Chircop, first to show dynamin II gene is a new target for cancer therapeutics
2010 – With Adam McCluskey, report several large studies of new dynamin inhibitors for epilepsy and cancer treatment, inhibitors now widely used in labs across the world
2011 – Toolkit of dynamin inhibitors licensed to Abcam Plc for commercial sales for researchers
2012 – Identification of the signalling control point for neuron branching and development. Launched the first ACRF Centre for Kinomics, with Prof Adam McCluskey, to accelerate therapeutic drug discovery

What’s Next

Pre-clinical trials for dynamin inhibitors and ring stabilizers in epilepsy, kidney disease and infectious disease.
“Children’s Medical Research Institute is important because they’ve allowed me to think on a bigger scale.

When I was first recruited to CMRI, I had been focused on one year blocks of time (what I could fit into a research paper), or on two or three year blocks (what could fit into an NHMRC Project grant application). When former Director of CMRI, Professor Peter Rowe, recruited me, he said, “Start by thinking in 5 year blocks. This strategy is that of a Program not a Project.”

Instead, I decided to form a 20 year plan instead.

In my first five-year grant application, I decided to plant the seeds for a twenty-year program. I said I would create the first pharmacology for endocytosis and dynamin. It was ambitious, and I had no idea how long it would take. Turns out it took 16 years.

Now, the pharmacological toolkit we created for studying dynamin and other proteins involved in endocytosis is in high demand by researchers around the world who are working to understand brain function and cell signalling. In order to meet demand, the toolkit was licensed to Abcam in 2011 for international research sales.

The questions that drove me at the start are the ones that still drive me today: How do nerve terminals work? How do they wire together to make the brain work? How are those signals carried from one neuron to another? Are these systems part of the cause of brain disorders? Curiosity drives me. Along the way, I developed pharmacological tools for studying nerve terminals, and it just so happens these are the source of revolutionary new treatments for epilepsy, neurodegenerative disorders, kidney disease, infectious diseases and cancer. Translation wasn’t the initial goal—it just happened as a consequence of meeting that first 20-year target.

Of course, now I have developed my second 20-year plan. I want to keep our new treatments progressing toward the clinic. I’m concerned with making medicines that work, and so we keep bettering ourselves. We often patent one therapeutic, but then we make something better the next year, and it’s not worth the cost to keep patenting them, so we let the patents expire. Only when we have something of high potency and solubility that we’re really happy with will we patent again. At that point we’ll work with a pharmaceutical company to bring it to clinical trials—and we’re nearly there. Of course, I want to be on the scientific board of that company, so I can give advice all the way to the end. I want to see the second 20 year plan realised as new treatments for epilepsy and cancer.”

Professor Phillip Robinson
Established May 1990

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

What They Do

Study how development occurs in order to understand what goes wrong in birth defects. Current focus is on genes involved in head and gut development.

Major Achievements:

1987 Published ground-breaking study showing how different types of mesodermal tissues are generated in mouse embryo. First step towards fully elucidating the blueprint of development in the mouse.
1990 Embryology Unit formed at CMRI
1992 Elucidated the developmental fate of tissues contributing to the backbone and muscles, using novel transgenic cell markers.
1993 Developed powerful experimental tool to study patterns of X-chromosome inactivation, aiding studies of Turner Syndrome.
1995 Seminal lineage tracing studies on the morphogenetic interaction and fates of tissues of the head and face.
1996 Demonstrated that germ cells in mouse embryo are not pre-determined but most undifferentiated cells in the embryo have the ability to form the germ line.

1999 Demonstrated that a specific population of cells acts like the organizer (identified previously in frog embryos by Nobel laureates Spemann and Mangold) which possess the ability to guide other embryonic cells to form a new embryo. This work and the germ cell study of 1996 were cited for Professor Tam’s election to the Fellowship of the Royal Society of London (2011).

2002 Completed a series of investigations of the role of the Twist gene in the development of head, face and limb, revealing the developmental basis of Saethre-Chotzen Syndrome.

2004 Discovered that a single-gene defect of platelet-derived growth factor C (PDGF C) could cause cleft lip and palate.

2006 Established the association of Mecp2 deficiency with learning and cognitive deficits and motor disability in a genetic mouse model of Rett Syndrome, a developmental neurological disorder in the hippocampal brain region.

2008 Identified two key genes for gut development, which provided an entry point to developing cell-based therapy for diabetes and OTC liver disease.

2008 Demonstrated that Rett syndrome is associated with a defect of Purkinje cell production in the brain. Showed that progression of Rett syndrome could be delayed by physical exercise and environmental enrichment.

2009 Completed the fate mapping of early mouse embryo.
2011 Demonstrated a stringent requirement to control the level of WNT signalling for normal head formation.

2012 Collaboration with the Cancer Research Unit showing that the ALT mechanism of telomere maintenance found in cancer cells also operates in normal tissues in mice.

What’s Next

Develop cell-based therapies for diabetes and OTC liver disease; further our understanding of the molecular switches and signals needed to control cell differentiation and predict the path of differentiation; expand efforts to find treatments for eye diseases; build a basic and clinical program to turn genetic and developmental biology research into treatments for craniofacial and dental defects.
“Over the years, one major accomplishment of my team has been the elucidation of the basic body plan of the mammalian embryo. This effort has occupied most of the last 28 years and was finally accomplished in 2009. Through these studies, we learned about the array of building blocks of the body of the foetus, in the context of the founding cell populations that will give rise to various major body parts. Other laboratories around the world have carried on, based on the knowledge gleaned from our studies, to refine the body plan further. Our aim is to move on to studies that apply this knowledge to the understanding of prevalent birth defects.

Through the course of working on the basic body plan, we came to understand how progenitor cells differentiate, and we now have a deeper understanding of the molecular signals and switches in the genetic regulatory network that guide a cell with many fates into a specific cell type. Going beyond the differentiation of individual cells, we explored the behaviour of a community of cells with different fates, in order to understand modelling of tissues and early organ formation.

This knowledge of the genetic mechanism of normal development and what may have gone wrong with congenital malformations will help our clinical colleagues understand birth defects they encounter in the clinic. While most birth defects are likely caused by many genes (polygenic) and modified by environment (multifactorial), we have shown that a single genetic defect can impart an overwhelming effect on development, as we showed with cleft lip and palate.

One major research area in the future is understanding genetic mechanisms affecting head development. We choose to study the most dramatic birth defects that don’t show up in the clinic because they are lethal, based on the rationale they could lead us to identify the cornerstone or most critical factors for normal development. This is an important prerequisite step in the discovery process. When we identify a cornerstone gene that is absolutely required to have a head, for example, we can then look at a cascade of genes linked to it, see how they are connected and how each contribute to the problem. It’s after this that we can think about prevention or management of birth defects. Gene therapy isn’t feasible now, as we can’t correct every cell, but signalling pathways can be modified by therapeutic agents to treat or prevent birth defects. Retinoic acid (a metabolite of Vitamin A), for example, affects signalling pathways, and too much of it causes defects in embryonic development. Modulating this activity may offer a means to prevent birth defects. It is our hope that supplements or therapeutics that could be used to prevent or treat specific types of birth defects will be identified using the knowledge of the role of these signalling factors.

Understanding the cellular and molecular mechanisms underlying the morphogenesis of the embryonic gut and associated organs (liver and pancreas) is another major area of current research. We’re working in collaboration with our Gene Therapy Unit to develop cell-based therapies to treat inherited liver disease, and we’re hoping to be able to grow pancreatic islet cells to treat diabetes.

Over the next 10 years, I’m hoping to set up an interactive basic research and clinical program here at Westmead that will combine information from the clinic with knowledge of genetics and developmental biology to find new diagnostic protocols and potential therapies for craniofacial and dental defects. It would be the first of its kind in NSW, and would help us achieve our goal of moving scientific knowledge towards developing treatments in the clinic.”

**Professor Patrick Tam**
Gene Therapy Research Unit

Established January 1995

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

What They Do

The Gene Therapy Unit finds ways to correct genetic diseases in children. Clinical trials are underway to correct SCIDX1-deficiency (“boy in the bubble” disease) and to improve chemotherapy treatment of paediatric cancers. They are currently working toward a new clinical trial to correct inherited liver disease.

Major Achievements:

1992  Ian Alexander undertakes post-doctoral training in USA to become expert in gene transfer technology
1995  Gene Therapy Research Unit formed, a joint initiative of CMRI and The Children’s Hospital at Westmead
2000  Establish clinical grade gene transfer vector production capacity in Australia
2002  In collaboration with the Children’s Hospital in Paris, conducts first ever gene therapy clinical trial for a genetic disease in Australia
2009 – 2011  In collaboration with the Australian pharmaceutical industry, prepared a gene transfer vector and anti-cancer drug formulation for paediatric clinical trial use

What’s Next

Clinical trials for genetic metabolic liver diseases.
“During my paediatric medical training I became interested in genetics and went on to do a PhD in molecular biology, as well as completing medical genetics training. From the start I was intrigued by the possibility of treating genetic disease by repairing the underlying genetic defect, but understood that the key challenges were technological, most notably the challenge of repairing or replacing faulty genes with healthy copies. So I travelled to the US to undertake post-doctoral training in gene transfer technology under Dusty Miller, who was at the forefront of research in the area and whose vectors had been used in the first ever gene therapy clinical trials (conducted by the US National Institutes of Health in 1989).

I learned an immense amount from Dusty, but his lab was working with vectors based on retroviruses and had shown that these vectors require cells to be dividing for effective gene transfer. Most cells in the human body aren’t—they are ‘post-mitotic’. I therefore started working on adeno-associated virus (AAV), which proved capable of genetically modifying non-dividing cells, and, with colleagues in Dusty’s laboratory, made a number of important contributions to the field at the basic science level. This is when I began my current work developing and exploiting gene transfer technology with a focus on treating genetic disease in children, especially involving the liver and bone marrow.

In 1995, CMRI and The Children’s Hospital at Westmead decided to form a gene therapy group, which I was fortunate to be invited to join in a leadership role. This gave me the opportunity to lay the foundations for a research effort focused on translating progress in the laboratory through to improved treatments for infants and children. Our strategy is to do the pre-clinical work at CMRI and the translational work at the hospital. We combine our own pre-clinical progress with the best available methods and technologies developed globally, and work to progress these towards clinical trials, often as part of an international collaborative effort.

Translational research is difficult and necessitates a broad range of skills and specialised infrastructure, including clean-rooms where gene transfer formulations can be produced and human cells can be genetically repaired in a sterile environment. Establishing such an environment took over 10 years, but we now have them and are in a strong position to make globally significant contributions to the gene therapy field.

Most importantly, we are now in a position where we can bring the world’s best advances in the field of gene therapy to Australian children at the earliest possible time.

We are excited by what’s been achieved and look to the future with great hope!”

Professor Ian Alexander
Dr Mark Graham is a Group Leader and part of the Cell Signalling Unit. He’s also a father of four, two of them twins, and all of them born since he started at CMRI in 2002.

“Work/life balance can be difficult,” Mark says, “especially as science is so demanding, but children do make you remember why research is important.”

Mark’s research focuses on a fundamental question: “Why and how do we get small packets of neurotransmitter in vesicles in the brain?” It’s probably not the first question most people think about when they wake up in the morning, but it is important for understanding how nerve cells communicate, for understanding learning and memory, and for finding new treatments for conditions as varied as Alzheimer’s disease and childhood leukaemia. Vesicles are structures that bud off of a cell membrane and carry things into or out of cells, anything from chemical signals telling the cells how to behave to invading viruses.

“Right now I’m interested in two clathrin assembly proteins, AP180 and CALM, both of which assemble clathrin coated vesicles.” Clathrin is a scaffolding material, a sort of microscopic version of a geodesic dome or piece of playground climbing equipment, that gives many vesicles their shape and helps them form.

“The AP180 protein is only found in brain and forms small vesicles in the synapses of neurons. CALM is found in all cells of the body and forms vesicles twice the size. You’d assume my interest in brain would make AP180 most appealing, but it turns out CALM has implications for both Alzheimer’s and leukaemia, and it’s captured my attention.”

When you examine aggressive childhood leukaemia, you will find many have a genetic mutation, a rearrangement of chromosomes that alters the CALM protein. “We think CALM is what makes these cancers more aggressive,” Mark says. “CALM is needed to transport iron into blood cells. These leukaemias have too many immature blood cells with little iron, so CALM is needed to transport iron into blood cells. These leukaemias have too many immature blood cells with little iron, so CALM is needed to transport iron into blood cells. These leukaemias have too many immature blood cells with little iron, so CALM is needed to transport iron into blood cells. These leukaemias have too many immature blood cells with little iron, so CALM is needed to transport iron into blood cells. These leukaemias have too many immature blood cells with little iron, so CALM is needed to transport iron into blood cells. 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Polymorphisms in CALM (small mutations in the gene) have also been found in Alzheimer’s patients. “It may be that CALM is needed to clear the junk from brain cells. CALM probably has a role in transferring these deposits through the blood brain barrier in endothelial cells. If CALM isn’t working, plaques build up over time to cause late-onset Alzheimer’s. CALM is also known to be involved in amyloid precursor protein (APP)-trafficking, so it could also cause Alzheimer’s by bringing more APP into brain cells where it can break down and eventually form plaques.”

“We still need to discover how CALM works, but it is likely to be important in any disease where transfer of material between the blood and an organ is important (e.g. blood to kidney, in kidney disease),” Marks says, “so my goal is to find subtle ways to regulate endocytosis and modulate its function to treat diseases. We find that most proteins simply can’t be turned on or off. They’re involved in too many processes, and turning something off to treat one disease may cause more problems elsewhere in the body, especially with CALM, which is found everywhere.”

“Post-translational modification, which is the addition of other molecules to a protein, is a much better way to subtly affect a protein’s function. There are many types of post-translational modification (phosphorylation, acetylation, sumoylation, methylation, ubiquination) and these can be studied and used to determine the fine controls for a protein and for disease treatment.”

When Mark started at CMRI in 2002, they had one mass spectrometer to work with (an extremely specialised machine to help study proteins and post-translational modifications at the molecular level). Together with Val Valova, Manager of the Biomedical Proteomics Facility, and Prof Phil Robinson, Facility Director, Mark has helped to build up the facility over time, and now they have seven mass spectrometers.

“We just completed a broad study of phosphorylation-based signalling in axon terminals,” Mark says. “This is where neurotransmitters are waiting to be released. The endocytic machinery sits there waiting to make vesicles. The only thing stopping it is phosphorylation, acting as chemical switches. We asked where are the sites of phosphorylation? Which ones are important for nerve signalling, which ones respond to a stimulus? Our most unexpected finding was that there were some phosphorylation changes that could last up to seven minutes. This is a long time in the neuron, where most signals are complete in seconds. This could be important for plasticity, for learning and memory. The longer a signal is carried, the more neurotransmitter is released, and the more likely the brain is to see it as a useful connection between nerve cells. A stimulated neuron is more likely to be stimulated in future, and this is the basis for learning and memory.”

The questions are many and varied, but his toolkit to answer those questions remains the same: mass spectrometry. “But,” Mark says, “bioinformatics is becoming more important now. We have so much data from mass spectrometry that we need faster ways of processing and understanding the data. This will bring us closer to clinical outcomes faster.”

When asked what he thought about the importance of basic research and the current trend towards clinical-focused work, Mark says,

“We need ‘Super Teams’ able to do basic research and link it all the way to the clinic, to patients. We can’t do it without basic research—we need new avenues and discoveries—but the same people can’t necessarily take it to the clinic. Achieving a vision for a cure requires collaboration.”
In addition to accelerating research efforts within CMRI and the Westmead Hub with facilities such as the Bioinformatics Unit, CMRI provides important resources for scientists throughout Australia. It operates CellBank Australia™, the only national repository of cell cultures, necessary for many fields of medical science. In addition, CMRI houses a major Biomedical Proteomics facility and 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.
Human or other 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 critically important 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 testing to confirm their integrity, and then distributes the cell lines to researchers throughout the world.

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

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

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

CellBank Australia receives funding from the Cancer Institute NSW and was also the recipient of a National Health and Medical Research Council Enabling Grant from 2005 to 2010. 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.
CellBank's Origins

"I agreed to work on CellBank in a taxi - as you do," says Dr Amanda Capes-Davis, who joined CellBank in 2005 and helped to establish the facility. "Roger Reddel [Director of CMRI] and I were in Melbourne working on another project and were sharing a ride from Melbourne airport. He told me about the idea he’d been working on. His lab and others were very aware of problems with cell line misidentification, but getting access to authenticated cell lines could be logistically difficult. Cells had to be ordered from cell banks overseas and, because the cells needed to be transported on dry ice to keep them viable, shipping costs were prohibitive. Orders were pooled to reduce costs, but that meant longer wait times. Also, Customs delays could cause whole shipments to be ruined. Roger was getting many requests for his cell lines from Australian researchers, and so he decided we needed an Australian cell bank to distribute cell lines locally.

“When I came on board, Roger had already gone through the long process of obtaining funding from NHMRC, Cure Cancer Australia and the National Breast Cancer Foundation. A wing had just been built onto CMRI with space we could use, so construction was the next challenge. Roger had a clear idea of what he wanted—positive air pressure and HEPA filters—based on his extensive cell culture experience. The air conditioning requirements were going to be significant anyway, so we decided to go further and create “clean-room” facilities. That meant it needed minimal dust build up – for example, no ledges on doors – so we brought in a specialist architect to help design it. The same architect is helping with CMRI's current building expansion program.

“Professors Bruce Robinson and Richard Lake from the University of Western Australia were the first to deposit cell lines with us. They were studying mesotheliomas and had an important collection derived from patients exposed to asbestos. Richard Lake is now a part of our Scientific Advisory Committee, and both he and the other Committee members are strong CellBank supporters.

“To be really useful, CellBank Australia needed to supply commonly used cell lines. We contacted ECACC in the UK, one of the major cell banks internationally, and they sent someone out to inspect our facility before agreeing to set up a co-distribution agreement with us.

“We’ve gathered unique cell lines from Australian researchers, so we also have a collection that isn't available anywhere else. There’s no predicting which lines will be useful, but we hold on to them in the expectation that in the future the research community will need them, allowing us to also recoup the costs over time."

“It was a big project to set up: making use of CMRI's expertise in cell culture and building management, bringing in quality control and assurance, database tracking, the website, and business aspects. I was brought on board to be across it all and to draw on whatever expertise was needed to make sure each aspect was the best it could be.”

When asked why she stepped down from managing CellBank, Amanda says, “It was a full time job, and my father needed support after having major brain surgery for Parkinson’s, so I switched to part-time and handed management over to others. I already had confidence in our technical staff: Elsa Moy who is an experienced cell culturist trained in Roger’s lab and who has a fantastic common sense approach to dealing with problems; and George Theodosopoulos who is one of the best in the world at STR profiling and cell line authentication.

“I still remained very committed to CellBank, and at home I spent 6 months developing a database of misidentified cell lines, which I knew would be useful to researchers. I trawled through research papers from the 1960s, from websites... and then just as I finished, Ian Freshney of Glasgow University published his database! But there were lines missing from each, so we combined our databases to work together. We now have a volunteer group of 17 distinguished scientists, called ICLAC (International Cell Line Authentication Committee), who keep the database up to date and hunt down authentic stocks around the world.”

When asked what Amanda wants to see in the future, she says, “I want journals to make cell line testing mandatory and for it to be as easy as possible for researchers to comply. It’s the best way to ensure the integrity of cell line-based research.”

About Dr Amanda Capes-Davis: She 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, and she is the Chair of the International Cell Line Authentication Committee; their database of misidentified cell lines can be found at www.cellbankaustralia.com.au
Bioinformatics is the application of information technology to the study of biology and medicine. Modern molecular biology research uses a variety of techniques such as genomics (large scale sequencing of DNA) and proteomics (large scale identification and characterization of proteins by mass spectrometry) that generate vast volumes of data. Sophisticated computational techniques are needed in order for the data to be correctly acquired, stored, managed, visualized, analysed, and interpreted. Bioinformatics is essential to modern health and medical research and needs to be an integral component of most biological research groups.

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

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

CMRI Bioinformatics will also play a key role in developing and establishing bioinformatics capability within the Westmead Research Hub and will work collaboratively with other bioinformatics initiatives throughout NSW and Australia.

**Associate Professor**

**Jonathan Arthur**
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-CFK). Currently the facility houses a total of seven fully functional mass spectrometry systems providing a massive increase in capacity and capability.

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.

The facility established an exciting scientific partnership with AB SCIEX in early 2012, with results presented in two posters at the Lorne Proteomics Conference in February 2013.

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 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.

Example 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 cell 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 medicines to potentially treat epilepsy and to greater understanding of nerve communication that may one day lead to treatments for other nerve disorders.
The ACRF Centre for Kinomics™

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

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

This significant, not-for-profit initiative builds upon demonstrated research excellence, leadership and successful collaborations between scientists from CMRI and UoN. The ACRF-CFK is equipped with state-of-the-art instrumentation, thanks to generous funding from the Australian Cancer Research Foundation (ACRF) and the Ramaciotti Foundations.

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

Collaborations have 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, and perform quality control and sample analysis for collaborating research teams.

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 molecular targets for the development of new cancer treatments 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.
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.

Fundraising

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 2012 and acknowledge supporters who gave generously of their time and money to help create a healthier, brighter future for all children.
Jeans for Genes®
Campaign
Jeans for Genes is one of Australia's most recognised and loved charity campaigns and is the major fundraiser for Children's Medical Research Institute.

Public support in 2012 was as high as ever with over two million Australians wearing their jeans on the first Friday of August in support of CMRI and its vital research work into childhood disease. Over $2.25 million was raised thanks to the help of an army of volunteers, supporters and corporate partners. Jeans for Genes has raised more than $60 million over the past 19 years.

Jeans for Genes 2012 set out to not only raise funds but link the fundraising event with the cause behind the day. This year ‘Kids took over Jeans for Genes’ lending their enthusiasm and significant pester power to encourage adults and other kids to ‘Get your Jeans On’ and also spread the message... ‘1 in 20 kids is born with a genetic disease but 20 out of 20 kids want to help find a cure’. Over 1,100 schools took part, raising $300,000, and just under 6,000 individuals helped generate over $1.09 million by selling merchandise and collecting donations from family, friends, workmates and the public. A number of retail partners including Big W, Westpac, Gloria Jeans, Newcastle Permanent, HCF and Lowes were joined by Woolworths to contribute nearly $680,000 in merchandise sales across hundreds of outlets throughout Australia.

The 2012 campaign culminated with its annual Gala Dinner attended by 450 guests who generously purchased tickets to the ‘Neverland’-themed magical event and bid for donated prizes, including the hallmark of the gala dinner, signed celebrity jeans from such well known names as Pink, Rachel McAdams and Anthony Warlow. The night was a huge success and generated $170,000 for CMRI, thanks to our guests and major sponsors, including Burwood Press, Sofitel Productions, Decorative Events and Liquor Marketing Group.

The Jeans for Genes campaign will be celebrating its 20th Anniversary in 2013 with a fresh range of merchandise and will continue to link jeans for Genes to CMRI’s work by placing greater emphasis on promoting the ‘1 in 20 kids...’ message. Schools are also being encouraged to contribute even more enthusiastically by introducing merchandise for the first time in many years to mark our 20th year. With the support of more volunteers, donors and retail partners, Jeans for Genes will provide significant fundraising for CMRI as it expands and make possible the world-leading research its scientists undertake.
Community Fundraising

CMRI relies on the devoted support of community groups and individuals, who host a wide range of fundraising activities and events, such as the annual Morgan Lewis Golf Day 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 2012, were:

- Bill Waugh Memorial Cup Tennis Day
- Canberra Committee’s Annual Luncheon
- Canberra Committee’s Celebration of the 50th Anniversary of Australian Ballet
- Hills Committee’s Mothers’ Luncheon
- Hills Committee’s Race Day
- Strathfield Committee’s June Gala
- Wagga Wagga Committee’s Christmas Fair
- Gosford Committee’s Glitzy Denim Dinner
- Melbourne Cup luncheons, sweeps and raffles held by Kangaroo Valley, Racquet and Northern beaches committees
- Golf Days – hosted by Vaucluse, Northern Beaches, Strathfield Committees
- Tennis day – Vaucluse Committee
- Card Days – Racquet, Northern Beaches Committees
- Quiz Night – Strathfield Committee
- Discovery Day catering – Beecroft Committee

Other wonderful community supporters also include: Trivett Class BMW Parramatta, with 10 years of support for the Golf Day; Rotary Club of Cessnock Wine Country; and Treasury of Craft, with 20 years of dedicated fundraising via craft stalls.
Jump for Genes™

The Jump for Genes program is bigger and better than ever, with over 50 jumpers signing up to skydive and raise funds for CMRI.

A recent highlight was mum, Kirsti Matby, who chose to skydive in honour of her youngest daughter, Livia, who was born blind, has autism, global developmental delay and scoliosis. Against all odds, Livia is now walking and has started saying some words. It is not known what caused Livia’s condition, but her family is passionate about medical research and the impact it can have on future generations of children.

Kirsti skydived alongside 76-year-old Elizabeth Bryan, a member of the Children’s Medical Research Institute’s Gosford Committee and mother to Dr Tracy Bryan, a Research Unit Head at CMRI. Together, Kirsti and Elizabeth raised almost $5,000, which will go towards understanding the causes of genetic diseases affecting children like Livia.

Jamm for Genes®

The Blue Mountains Country Jamm for Genes held in January showcased the cream of Australia’s young country music stars, who donated their time and talent to raise money for Jeans for Genes.
**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, Mr James Fairfax, Mrs Joan M Barnet, Hunter Hall, Woolworths Support Office Bella Vista, Franklins, and J.J. Richards & Sons.

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

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

We are incredibly grateful to Kimberly-Clark for long term support of CMRI since 2006, which has seen significant contributions to our research programs via the Kimberly-Clark Research Fellowship, generous support of CMRI’s national Jeans for Genes campaign, the support of our Science Education program and the generous provision of Kimberly-Clark products for use in our research laboratories. The direct dollar value contribution to CMRI over the term of our partnership, which concluded at the end of 2012, was around $1 million. Thanks a million Kimberly-Clark Australia!

Some of our corporate supporters provide a combination of pro bono services and financial sponsorship. Particular thanks goes to Westpac, Technology One, Addisons Lawyers, Allens>Linklaters, and AB Sciex for their generous support throughout 2012.

In the year ahead, we will continue to develop new and existing partnerships, and look forward to seeing what we can achieve together in 2013.

**Community Partner: Sydney FC**

Sydney FC and CMRI are now in the second year of an agreed three-year community partnership, which was launched in February 2012 when Sydney FC took on Perth Glory and won! CMRI will benefit from the partnership through awareness and fundraising campaigns, as well as the ambassador program. Current Sydney FC ambassadors include Socceroo, Brett Emerton, and Sydney FC defender, Pascal Bosschaart.

Brett spent a day with scientists at Westmead in 2012 learning about the research being carried out by CMRI.

“Spending time at CMRI really opened my eyes to the great work that is done by extraordinary Australians trying to give all of us a better quality of life,” said Brett, who is the father of two boys. “The scientists doing this research are the real heroes and it is very humbling to think that they go to work every day trying to work out how to save people’s lives.”

Brett and Pascal spent the morning of Jeans for Genes Day in Martin Place to help raise awareness. They also showed their support for CMRI in an interview conducted by the Channel 7 Sunrise team.
Why Allens supports CMRI

The first Jeans for Genes Day at Allens was almost 20 years ago in Sydney. Partners and staff in this major law firm broke away from their regular formal suit attire and wore jeans to the office in support of Children’s Medical Research Institute.

Each year more and more staff and partners have enthusiastically embraced the fun theme of the day and generously supported the fundraising activities at the drinks function at the end of the day. Each of the offices in Melbourne, Brisbane, Perth and Sydney have their own themed fundraising events ranging from a ‘battle of the bands’ and Australian Idol-type event in Sydney and Melbourne, to other fundraising activities in Perth and Brisbane.

“The research which the dedicated teams of doctors and researchers are doing at the Children’s Medical Research Institute is invaluable and we at Allens are proud to be a long standing supporter of the CMRI, both through our charity committee and our pro bono legal work.”

(Jim Dwyer, Chairman Allens Charity Committee)

About Allens

Allens is an international law firm with offices throughout Australia and Asia. On 1 May, Allens formed an integrated alliance with the international firm Linklaters. This has resulted in the two firms working together closely for the benefit of clients around the world. Allens’ people are passionate about supporting their communities and environments, and they are the drivers of their Pro Bono, Charity, Environment, Reconciliation Action Plan and Asia Community Committees’ initiatives. Children’s Medical Research Institute and Allens have been working together for over 20 years through Allens’ Charity and Pro Bono Committees.

The Charity Committee

Allens has a specialist Charity Committee made up of partners and staff from its Australian offices. The Allens Charity Committee oversees the Firm’s interactions with charitable organisations and is responsible for the Firm’s donations and other charitable contributions.

“As a firm, we recognise that we have broad responsibilities – to our people, their families and the communities in which they live. We are privileged to have gifted and motivated people who want to make a difference, not only in the law and in business, but also in the wider community.”

(Michael Rose, Chief Executive Partner)

The Pro Bono Committee

Allens aims to have a coordinated, focused, well balanced and meaningful pro bono practice. The Pro Bono Committee has adopted criteria for pro bono work to ensure that the Allens pro bono practice assists people in need and causes that benefit the community. Their pro bono practice is very proud of its involvement with the Children’s Medical Research Institute on a range of corporate governance, corporate and commercial and intellectual property matters over the years.

“In many of our matters, we have worked closely with the board and senior executive of the Children’s Medical Research Institute, and I’ve always been impressed by their joint commitment and unremitting focus on the independence of and core objectives of the organisation.”

(Ian McGill, CMRI relationship partner, Allens)

Matched Funding Program

The Allens Matched Funding Program was launched in 2005 and is coordinated by the Charity Committee and the Pro Bono Committee. Under the program, Allens has an annual budget to match, dollar for dollar, donations made by staff to selected charities. The purpose of the Matched Funding Program is to facilitate philanthropy amongst staff, enabling staff to give regularly to causes they wish to support.
Before the late Mrs Claire Yass made her will, she reflected on the many positive things she might do with her estate. She considered gifts and bequests in various forms, appraising the work and worthiness of charitable institutes who are in constant need of funds to fulfil their important roles in society.

There was an area in which Mrs Yass was particularly interested – she knew she wanted to do something that would improve the lives of children. After her death in 1995, CMRI was contacted and advised of her $520,000 bequest. In discussion with the executor of her will, it was agreed to use this generous amount to fund a post-graduate research position in perpetuity, and the Yass Memorial Scholarship was established in 1998.

The first student to complete his PhD as a recipient of this scholarship was Dr Christian Toouli, working in our Cancer Research Unit, whose studies on the enzyme telomerase have given new understandings into the causes of cancer. CMRI remains hopeful that this continued research will lead to new, less toxic and more effective treatments for cancer, and ultimate prevention of the disease.

The current holder of this scholarship is Ms Claire Deakin, working in our Gene Therapy Unit, who is helping to improve the long-term safety and efficacy of gene therapy treatments for SCIDX1-deficiency (where a single genetic change results in a child being born without an effective immune system). Clinical trials for this disease, conducted by the Gene Therapy Unit, are currently underway and Claire's work will contribute to reducing side effects from the treatment.

The late Mr and Mrs Yass both came to Australia from Europe in 1938, and her husband, Mr Emery Yass, established Tennyson Textiles, a successful, local manufacturer of fabrics. It later became a publicly listed company and was eventually purchased by Dunlop.

Mrs Yass has left a lasting legacy – a commitment to research is an investment in the future with the potential to ensure an improvement in the lives of many children affected by disease.
Our Redevelopment

CMRI has initiated plans for a redevelopment on our existing site to provide us with the space and requirements needed to maximise our research potential and take our discoveries to the next level for the benefit of children and their families.
Our current building is at capacity and needs to expand in order to support our expanding research efforts, accommodate greater student intake, provide improved infrastructure for specialised technologies, and allow space for our growing national facilities. In addition, many of our core research programs are reaching developmental stages that will greatly benefit from greater depth and breadth of research and support staff, leading to better and faster translation into health outcomes.

Our proposed redevelopment is part of ongoing development plans for the whole Westmead precinct, all of which will create a world-leading centre for health and medical research. The precinct will be better able to pool resources, sharing access to cutting edge equipment and increasing the potential for inter-disciplinary collaboration.

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

We held a ‘Turning of the Sod’ event on 12 November, 2012 to mark the start of construction preparations, and the first stage of the build, contracted to AW Edwards, is now well underway.

The first stage is a tower in our front courtyard that will increase our capacity by two thirds. We expect to complete this construction in 2014 and are seeking additional funds from private and other government sources to help reach that target. A second stage will then commence, provided a further $38m of funding is committed.
Westmead Research Hub and Precinct

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 Hub collaborate, sharing knowledge and expertise. The Hub also coordinates the purchase and sharing of major equipment.

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 at 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 for major Australian research efforts.

The Westmead Precinct also includes the Westmead Private Hospital and Cumberland Hospital, all of which combined makes Westmead the largest Health and Medical Research Precinct in Australia.
Finance and Governance

CMRI is an independent research institute based in Westmead, NSW. The Institute employs approximately 160 people, including 120 full-time scientists and PhD students, as well as operational and administrative support staff and a team of fundraisers. The organisational structure of CMRI reflects its corporate governance and areas of responsibility.
Board of Directors

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

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

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

Directors in Office are:

**Professor Frank Martin MSSS 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 American Academy of Ophthalmology and the International Council of Ophthalmology (ICO) and has recently been appointed Director of Society Development and Leadership for the ICO. He is the Vice Chairman of RANZCO Foundation and was President of the Royal Australian and New Zealand College of Ophthalmologists from 1996 to 1997. He is also Chairman of the Westmead Research Hub and on the Board of the Lowy Medical Foundation. Professor Martin has been a CMRI Board member since 1986 and elected President in April 2000. Professor Martin serves on the Institute’s Audit and Risk Committee, Finance and Investment Committee, Intellectual Property Committee and chairs the Nominations and Remuneration Committee.

**Mrs Carolyn Forster (OAM), Vice President**

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

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

She received an ACT Women’s Award in 1996, a Centenary Medal in 2003, and an OAM in 2006. Mrs Forster joined the Board in 1996 and was elected Vice-President in 2000. Mrs Forster serves on the Institute’s Finance and Investment Committee, Audit & Risk Committee and Nominations & Remunerations 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 QBEI Mercantile Mutual Limited. He is an actuary by profession and is a former President of the Institute of Actuaries of Australia and is a Life Member of that Institute. He has been a director of a number of public companies, APRA, a number of industry bodies and was Chairman of Macquarie University Actuarial Foundation. He has been involved in several task forces and advisory bodies to federal government. Currently, he is a director of Hannover Life Re and ING Bank Foundation. Mr Atfield’s extensive experience in actuarial management and financial administration led to his appointment to the Board of CMRI in February 2001 and election as Treasurer in December 2001. Mr Atfield chairs the Institute’s Audit and Risk Committee and Finance and Investment Committee. He is also a member of the Intellectual Property Committee and the Nominations and Remuneration Committee.

**Mr John Bevins**

Mr Bevins is former Creative Director of the independent Australian advertising agency, John Bevins Pty Limited. His agency was established in 1982 on work that included NSW’s highly successful anti-smoking and Random Breath Testing campaigns, and closed its doors in 2010. Jeans for Genes® was an initiative of the John Bevins agency, created in a brainstorm with scientists from the Institute.

In 2001, Mr Bevins was awarded the inaugural Advertising Federation of Australia medallion for his contribution to the advertising industry. He has been a member of the CMRI Board since 1986 and was a member of the Institute’s Audit and Risk Committee. Mr Bevins resigned as a Director of the Institute on 4th March, 2013.

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Professor Kathryn North AM MD BSc (Med) FRACP
Kathryn North was Head of the Institute for Neuroscience and Muscle Research and Associate Dean of the Clinical School, The Children’s Hospital at Westmead. She was also the Douglas Burrows Professor and Head of the Discipline 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 Sunderland Award for achievement in neurobiological 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. Professor North is past Chairman of the Children’s Hospital Research Laboratories Committee and an Executive Board member of the World Muscle Society. She was a member of the Children’s Hospital Research Executive and Research Committee, and the University of Sydney Medical Deans Advisory Committee. She is Chairman of the Genetics Sub Committee of the Australian Association of Neurologists. She was appointed a Member of the Order of Australia in 2012. She joined the Board of CMRI in 2000. Prof North resigned as a Director of the Institute on 11th January, 2013 and moved to become Director of the Murdoch Institute.

Professor Ian Caterson (AM MBBS BSc(Med) PhD FRACP)
Ian Caterson is Boden Professor of Human Nutrition and Foundation Director of the Institute of Obesity Nutrition and Exercise, University of Sydney. Previously, he was Senior Staff Specialist and Director of Clinical Endocrinology at Royal Prince Alfred Hospital. He was a post doctoral researcher at the University of Oxford with Professor Sir Philip Randle FRs. His research interests have been in insulin resistance and the causes, prevention and treatment of obesity and the prevention of chronic disease.

He is a member of Newington College Council and chair of its Education Sub-Committee. He is a past president of the Australian Diabetes Society and the Australasian Society for the Study of Obesity. He was previously Head of the School of Molecular & Microbial Biosciences at the University of Sydney. He is on the management committee of the International Obesity Task Force and was a regional advisor on obesity for the World Health Organisation (WHO). He is Past President (Asia-Oceania) for the International Association for the Study of Obesity. He is an editor of Diabetes Obesity & Metabolism.

Professor Caterson joined the Board of CMRI in 2004 and is a member of the Institute’s Intellectual Property 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 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 1983-2007, Managing Director of Edwards Dunlop and Company Limited between 1978 and 1989 and Director of Health Super Pty Ltd between 2000 and 2007.

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; Non-Executive Director, SW Sydney Medicare Local Transition Board; Member, Central Sydney Planning Committee; Advisor, Investec Bank (Australia) Ltd; Director and Advisor, Inghams Enterprises; Director, Tulich Family Communities Aged Care; Independent Chairman, Prospect Water Partnership; Independent Chairman, Al 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). On 28 January 2011, Mr Knowles was appointed as the Chair of the Murray-Darling Basin Authority. Mr. Knowles is a Fellow of the Australian Property Institute and a Certified Practising Valuer. He joined the CMRI Board in May 2007.

Mrs Patricia Payne (OAM MPS PhC)
Patti Payne has been a Community Pharmacist for over 25 years, practising on the Central Coast, NSW. She joined the Beecroft Committee of CMRI in 1969 serving as President 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 Biosafety Committee and has been heavily involved with Jeans for Genes since its inception. She has served on the Board of Trustees of the Kings School Foundation and has organised many functions for other institutions and charities. She is the foundation President of the Women for Pharmacy network, Chairperson of the Events and Hospitality Committee of the Federation Internationale Pharmaceutique (FIP) World Conference, Sydney, 2003 and is the Australian nominee to the Board of Directors of the Community Pharmacy Section of FIP. She has four adult children. 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.

Clinical Professor Graeme Stewart (AM BSc(Med) MBBS PhD FRACP FRCPA)
Graeme Stewart was appointed as founding head of Immunology at Westmead Hospital in 1980. He is the inaugural director of the Institute for Immunology and Allergy Research, one of the four founding research groups of the Westmead Millennium Institute. Professor Stewart was the inaugural president of the Australasian Society for HIV Medicine and has played a role at a national and
Meet Jennifer Philips

Jennifer Philips, CMRI’s Community Relations Manager, says her job is, “To educate the public on our research. It will always be my first, most important job. It can be school kids, service groups, community groups… anybody. There are a lot of misconceptions and myths out there, and people value a clear explanation. Then they’re just fascinated and want to learn more.

“My job from the start was to translate between researchers and the public, giving presentations everywhere, talking, talking, talking in my best Scottish brogue. And meeting the nicest people in the world. It’s the best part of my job. I’m always meeting the nicest people from everywhere—Cessnock or Wagga or Burke or wherever, a church group or Rotary group—good, kind genuine people.”

Jennifer majored in genetics at University in Glasgow and has taught High School Biology all over the world—East Africa, South Africa, England and Australia.

“We were in South Africa,” Jennifer says, “and decided to seek a new challenge in Australia. I taught at Barker College, and it just so happens I taught both of PJ’s [Professor Peter Jeffrey’s, a former Unit Head at CMRI] children. When I hit the big 5-0, I decided to change careers. I did sales marketing for a biologicals company and CMRI was a client. I instantly fell in love with CMRI. It’s the honest truth. The emotion on the day I first stepped through those glass doors, a doopy little 50-year-old sales rep…the whole atmosphere was different from everywhere else. It was welcoming. I had a feeling of warmth.

“Even today,” she says, after having organised a magnificent Easter morning tea for the Institute, “that’s an important part of my job. Keeping us together. A family. Hopefully, we can continue to instil that culture of warmth and caring I first found here, instil it into the next generations coming through.”

When asked about her plans for the next 20 years and whether it includes retiring, she says, “No. Definitely not retiring. If I have the same energy levels in the next 10 years, it will be same old same old for me. Just as I like it."

“I love my job as much now as I did 20 years ago. I love the committees and the other fundraising groups I meet all the time. I’m fulfilled. I get the excitement of the researchers when they tell me ‘what if’, when they’re developing new knowledge and understanding. It also fulfils my creative side by coming up with ideas of how to express things better, to illustrate science, such as DNA made out of clothes pegs… analogies are important.

“I started Jeans for Genes 20 years ago with Stephen [Ryall]. It was just Stephen and me with wonderful pro bono support for the ads, PR, merchandise and decor, celebrity jeans and artists – just about everything. It was exciting and new and so many people were willing to help. I love to see how Jeans for Genes has grown. It’s got legs.

“Looking back 50 years, not just the last 20, I see that the Sir Lorimer Dods and Dr John Fulton legacy is still there and it makes CMRI unique. This is where it started. We haven’t changed. We still believe. Fifty years ago, we said ‘if only we could eradicate polio; if only we could eradicate these infectious diseases…’ and we have. Now it’s the next lot: cancer, blindness… Whatever it is, we will do it. If we don’t who will? We can’t just throw up our arms and say it’s too difficult. We can’t.”
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

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

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

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
Investing
In Their
Future
Financial Management

“CMRI can report another successful year of providing world-class medical research to the Australian community at funding levels that have increased on previous years. This research is funded by a mix of initiatives and capabilities, many of which have shown some improved performances on previous years.

Chief Financial Officer & Company Secretary: Ralph Mitchell

Our research grant income rose slightly over 2011 levels. Research funding can come from a variety of government and non-government sources, where individual projects compete for available funds, largely under peer-reviewed application processes. It is pleasing to see CMRI’s researchers continue to be successful in receiving funding, as it is an endorsement of the quality of the work being performed. Research grant funding is also earned to support the infrastructure of the research organisation (e.g. support services and building facilities) and to support equipment purchases, which are often highly specialised technologies fundamental to modern scientific techniques. In 2012, CMRI received a major contribution from the Australian Cancer Research Foundation to purchase several mass spectrometers, which were placed in the landmark ACRF Centre for Kinomics, a collaboration between CMRI and the University of Newcastle.

A major source of income for CMRI continues to be its fundraising, both in the name of CMRI and under the banner of Jeans for Genes. A strong community network of fundraising committees, plus our own dedicated team of fundraisers, conduct activities throughout the year, from large scale public events down to local town functions. Our largest event is Jeans for Genes Day, which has national media exposure plus volunteers and supporters from across the country. In 2012, fundraising revenue was also slightly increased on 2011 but did not match the increase in some of our costs, so the net contribution was down slightly. Some of these costs represent investment in growing our future fundraising revenues. 2013 will also be a building year, as we position the Institute for its own growth in the coming years. We continue to look at new initiatives to assist with funding this growth.

Our third major source of income is investment returns. Investment markets generally continued with some uncertainty in early 2012, but, by the end of the year, equity markets here and overseas had generated some strong returns. 2012 investment distributions received (including interest income) were not significantly different to 2011 levels; however, significant gains were recognised from redemptions during the year plus revaluations as at 31 December, 2012. This strong performance has continued into 2013, so we look forward optimistically to continuing our better than targeted investment returns. CMRI’s investments are monitored by a financially qualified sub-committee of the Board of CMRI, as advised by an independent investment adviser, and our financial assets are strategically allocated to a mixture of fund managers, experts in different investment categories. The combination of growth and defensive asset types provides a blended return commensurate with limiting our risk. In 2012, this overall return was 11.3%.

As mentioned last year, we hope to be able to support some of our research by generating more and more commercial returns from the use of our research intellectual property – mostly by licensing patents, or selling products and services using our trademarks and know-how. Some new activities were commenced in 2012, which we hope to add to and develop further in 2013. The amount earned from these activities in 2012 remained modest, but the future potential continues to grow as opportunities continue to be identified and further research work is performed.

A major contribution to our finances in 2012 was made by the New South Wales Government in the form of a special-purpose building redevelopment grant for $20m. This money was received in April 2012, and, after completion of detailed design work and a formal tender process, we appointed a construction contractor in February 2013. In the meantime, our financial results for 2012 show the portion of the $20m we consider earned in 2012 (approximately $2m), being the amount spent in the year on the building project. The balance of the $20m funds continues to be invested in term deposits and will be brought to account as income as it is spent on the project in 2013 and 2014.

I would like to take this opportunity to add my own thanks to the board and committee members, managers and staff at CMRI, as well as the many volunteers who fundraise on our behalf throughout the year. Each of their efforts related to the combination of income streams, each significant, has contributed to the development of a sustainable operating model where we can continue to fund and grow our research programs over long time horizons and sometimes in the face of very competitive conditions.

Ralph Mitchell
Chief Financial Officer & Company Secretary
April 2013
Sources of Revenue and Expenditure

**YTD December 2012**
- Total – $26 million
  - 41% Fundraising Income
  - 26% Investment Income
  - 25% Research Grants Income
  - 8% Building Redevelopment Income

**YTD December 2011**
- Total – $20 million
  - 38% Fundraising Income
  - 28% Investment Income
  - 26% Research Grants Income
  - 11% Building Redevelopment Income

Revenue
- Fundraising Income
- Investment Income
- Research Grants Income
- Building Redevelopment Income

Expenditure
- Fundraising
- Administration and Facilities
- Research

Statement of Assets

**Total – $111 million**
- 49% Current Assets, including cash and term deposits
- 16% Current Assets, including cash and term deposits-restricted use Capital Grant
- 19% Financial Assets
- 11% Property, Plant and Equipment; other non-current assets

**Total – $87 million**
- 70% Current Assets, including cash and term deposits
- 11% Current Assets, including cash and term deposits-restricted use Capital Grant
- 19% Financial Assets
- 7% Property, Plant and Equipment; other non-current assets
# Financial Summary

## Profit and Loss Statement

<table>
<thead>
<tr>
<th></th>
<th>YTD Dec 2012 (in $ ’000s)</th>
<th>YTD Dec 2011 (in $ ’000s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Revenues</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research</td>
<td>10,808</td>
<td>7,384</td>
</tr>
<tr>
<td>Fundraising</td>
<td>6,801</td>
<td>6,659</td>
</tr>
<tr>
<td>Investments</td>
<td>5,336</td>
<td>5,367</td>
</tr>
<tr>
<td>Capital Grant</td>
<td>1,986</td>
<td>–</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>24,931</td>
<td>19,410</td>
</tr>
<tr>
<td><strong>Expenses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research</td>
<td>15,588</td>
<td>14,607</td>
</tr>
<tr>
<td>Fundraising</td>
<td>3,125</td>
<td>2,423</td>
</tr>
<tr>
<td>Administration and facilities</td>
<td>4,942</td>
<td>5,069</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>23,655</td>
<td>22,099</td>
</tr>
<tr>
<td><strong>Surplus/(loss) before investment transactions</strong></td>
<td>1,276</td>
<td>(2,689)</td>
</tr>
<tr>
<td>Investment transactions, net</td>
<td>1,131</td>
<td>202</td>
</tr>
<tr>
<td><strong>Surplus/(loss) from continuing operations</strong></td>
<td>2,406</td>
<td>(2,487)</td>
</tr>
<tr>
<td>Other comprehensive income/(loss) from available-for-sale financial assets</td>
<td>2,526</td>
<td>(2,630)</td>
</tr>
<tr>
<td><strong>Total comprehensive income/(loss) for the period</strong></td>
<td>4,932</td>
<td>(5,116)</td>
</tr>
</tbody>
</table>

## Balance Sheet

<table>
<thead>
<tr>
<th></th>
<th>As at: 31 Dec 2012 (in $ ’000s)</th>
<th>As at: 31 Dec 2011 (in $ ’000s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Assets, including cash &amp; term deposits*</td>
<td>37,034</td>
<td>9,695</td>
</tr>
<tr>
<td>Other Financial Assets</td>
<td>54,086</td>
<td>60,901</td>
</tr>
<tr>
<td>Property, Plant and Equipment</td>
<td>18,408</td>
<td>14,959</td>
</tr>
<tr>
<td>Other Non-current Assets</td>
<td>1,238</td>
<td>1,238</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>110,766</td>
<td>86,794</td>
</tr>
<tr>
<td><strong>Liabilities</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Liabilities**</td>
<td>23,477</td>
<td>4,384</td>
</tr>
<tr>
<td>Non-current Liabilities</td>
<td>208</td>
<td>262</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>23,685</td>
<td>4,645</td>
</tr>
<tr>
<td><strong>Net Assets</strong></td>
<td>87,081</td>
<td>82,149</td>
</tr>
</tbody>
</table>

* Includes $18.7 million restricted for use under the Building Redevelopment Capital Grant Funding Agreement ** Includes $18.8 million of Deferred Income from Building Redevelopment Capital Grant received of $20 million

The above numbers have been extracted from the Audited Financial Statements of CMRI for the relevant periods. The full audited financial statements are available at www.cmri.org.au/Annual Reports
Thank You

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.