Thank you for helping us beat childhood diseases.

2017 THE YEAR IN REVIEW.
Foreword
From Professor Roger Reddel, Director of Children’s Medical Research Institute

2017 was a year when the ProCan® project accelerated, analysing the proteomes of more cancers than anyone has ever achieved before. And it was the year that more than 140 gene editing and therapy tools prepared here at CMRI were provided to over 40 national and international research groups.

Throughout 2017, government funding of medical research in Australia remained at an historic low point. However, because of your ongoing support, important research continued.

You helped fund equipment crucial to ProCan’s operation; you supported Professor Jamieson’s efforts to cure inherited blindness, and you aided Dr Scott Cohen in his search for the structure of telomerase, which will help develop new treatments targeting 85% of all cancers.

Your firm and continued support makes all the difference, and it will continue to make a difference long into the future when tomorrow’s kids will say ‘thank you’ for what you’ve done.

Here, in the Year in Review, you’ll find more information on what you’ve helped us achieve. Thank you.

Roger Reddel
Lorimer Dods Professor and Director
Children’s Medical Research Institute
Here’s what you’ve helped to achieve in 2017

ProCan scanned thousands of proteomes
and is well on its way to achieving its goal of analysing 70,000 cancers by the end of 2023

Over 50 families have been given a genetic diagnosis for their eye disease in hospital

The Vector and Genome Engineering Facility prepared over 141 tools
for genome engineering and gene therapy, more than 42 of those for external collaborators

Potential new drug treatments for kidney disease have been patented in 5 countries

Research spend by disease

| Disease         | 2017
|-----------------|------
| Cancer          | 41%  
| Embryology      | 21%  
| Genetics        | 25%  
| Neurobiology    | 13%  

total $ spend 13m

Jeans for Genes is celebrating its 25th anniversary in 2018

We’d like Australians everywhere to make jeans for Genes their charity of choice in 2018. The goal in our 25th year is to raise $25 million—enough to create new centres of collaboration, bringing world-leading research and hospitals together to help Australian kids suffering from genetic disease. We can do this.

Our sincere gratitude to everybody – the tens of thousands of Australians that get involved by purchasing merchandise or donating and all our loyal volunteers raising money on the day. We simply couldn’t do it without you!
Gene therapy helps clinicians globally treat a range of genetic and other diseases. But many hurdles remain before safe, effective gene therapy is available to all who need it, especially children.

In 2017, CMRI researchers made an important discovery (published in Nature Genetics) that will make gene therapy—which is already helping to cure genetic diseases—safer and more effective for children like Charlize Gravina.

Gene therapy is already helping patients internationally overcome genetic diseases like haemophilia. But gene therapy treatments still need to be tailored to the thousands of conditions where this approach offers the prospect of effective treatment. A lot of work remains.

Central to this work, in key organs such as the liver, are gene transfer tools used to replace or repair faulty disease-causing genes—AAV vectors. AAV vectors are like microscopic repair kits that can fix errors in DNA. They are being designed by Dr Leszek Lisowski and his team in CMRI’s Vector and Genome Engineering Facility (VGEF).

But when giving gene therapy to children, safety is a top concern. Professor Ian Alexander, Head of Gene Therapy, and his team have identified a small region in naturally occurring AAV that can sometimes have negative effects on liver cells.

"Initially, we were relieved to finally have a diagnosis," mum, Julie said. "Once we were told (more) we were completely crushed. We were absolutely devastated that our brand new beautiful twins would not have the normal life that we had imagined for them and that they deserved."

Isaac underwent surgery for a liver transplant, which would make enough of the missing enzyme to help give him a more normal life. But after surgery, a bacterial infection sent him into septic shock. Tragically, on 23rd January 2017, Isaac passed away. Now his twin sister, Charlize, is on the transplant list as she awaits a new liver.

"We look forward to a future where gene therapy would be available to completely cure our beautiful daughter, Charlize, and children like her, who are living with the most severe metabolic diseases," Julie said. "We just wish that future was now, so we wouldn’t have to expose Charlize to those same risks associated with organ transplant that ultimately took our precious boy."

"30% of infant deaths are due to genetic and congenital conditions. Things like this drive us. Anything I can do to help kids.”

- Dr Leszek Lisowski, VGEF

The discovery by Professor Alexander and his team will improve future gene therapy treatment. “Now we’ve identified this element, we can edit it out of our AAV vectors, which is important when clinicians want to treat brain diseases but not affect the liver, for example. This means increased specificity as well as safety.”

Prof Alexander’s work is part of a collaborative research effort within Paediatro™, a co-operative joint venture between Sydney Children’s Hospitals Network, Children’s Medical Research Institute, and Children’s Cancer Institute.

There are currently a 130 registered AAV clinical trials globally, with over 2000 patients treated so far, and this will only grow in the future. Professor Alexander’s work will help ensure that research produces safe as well as effective cures for genetic diseases. And the sooner such treatments are available for children, like Charlize, the better.
“Our epilepsy drug development program is a numbers game,” says Professor Phil Robinson, Head of the Cell Signalling Unit.

“We can devise potential new epilepsy treatments based on what we’ve learned about neurobiology, but hundreds of potential chemicals need to be screened before we find those with real potential.

“Fortunately, we’re now at a stage where we have some great drug candidates that work well preventing seizures in pre-clinical studies.

But we need to refine them for use in people. That means tweaking chemical structures, followed by trial and error, until we get there. But we will get there.

“All the work along the way isn’t wasted either. We’re contributing to global research efforts by licensing our early chemicals for research use. They are widely employed internationally, with 688 orders in 2016 and over 345 scientific research articles written which employ them.”

“Epilepsy is a neurological disorder where the pathways in the brain sometimes don’t connect properly, or they go a bit crazy, and there is a high level of activity in the brain, which gives you a seizure.

“Whenever I feel really dizzy, I know that I have about 30 seconds before I black out and have a seizure. That’s usually enough time to yell out to someone or sit on the floor, so I don’t hurt myself when I fall.

“Once I had a Grand Mal Seizure (a really big one) and bit my lip so hard it bled and swelled up. I never remember what happens. Once, I woke to all my family standing around my bed and paramedics in the hall. I wondered what everyone was doing there, and why they were all looking at me!

“I feel very strongly that I don’t want my epilepsy to rule my life.

“It changed my life when the medication wasn’t working. I was constantly tired. It took about two years to get the medication right. One of the drugs I tried gave me a very bad reaction: my legs became enormously itchy; it looked like a cat had used them as a scratching pole. I would cry in bed at night because I wanted to scratch them and I couldn’t sleep. Some drugs can affect the function of the liver and other organs, so I needed regular tests of my liver when I was on that drug, and I still had seizures.

“It’s the little things that make up life, and it’s the little things that I have to monitor or pay attention to. It’d be really good if I didn’t have to explain that I have epilepsy, and suffer the strange looks I sometimes get, or walk around seeing people notice my medic-alert bracelet then look at me like I’m contagious. It’s not fun having epilepsy. Many people have really severe epilepsy that ruins their lives. It’d be fantastic if there was some cure for the condition.”
A Children’s Medical Research Institute scientist has successfully reprogrammed stem cells in rabbits to resemble the early embryonic cells in humans. Research scientist, Pierre Osteil, had his work published in Stem Cell Research in 2017.

“Stem cells present amazing questions,” Pierre said. “An analogy I like to use is that you start with one cell after fertilisation and it’s just like the top of the mountain when the river starts to form, there are more and more branches. A turtle and a human start as one cell and look the same at the start, but what is the difference that makes them a turtle or a human?”

One aspect that Pierre has been focusing on is how to differentiate individual cells. “I wanted to go back to the development of embryos,” he said. “We all have the same DNA in our body, but each part of the DNA is so different. I want to know what is behind it. I want to understand which cells are growing to become the liver, for example.”

Pierre has worked with rabbits to make stem cells that resemble early embryonic cells. This is important for helping us understand how one cell “differentiates” into other cell types. This is the process through which a cell becomes specifically a liver or a muscle or other cell.

The kind of tool Pierre has created using rabbit cells helps us understand how birth defects occur in humans and how to prevent them, but it goes beyond that to enabling new treatments for diseases. Understanding how a cell becomes the retina of the eye, for example, allows us to grow a patient’s skin cells and turn them into retina for a transplant that cures blindness. Likewise, new liver cells can be grown to replace those affected by genetic disease.

“We are faced with such big questions and to answer them is so hard,” Pierre said. “We are answering smaller questions to start to build something stronger. I see myself as a builder.”

Thank you for telling us what matters to you

We are extremely grateful to those who completed last year’s survey, as it helps us keep you up to date on areas of research that are important to you.

Your top three motivations for supporting medical research:

1. I think that medical research is the only way new treatments and cures can be developed.
2. I want to accelerate the speed with which medical research can develop new ways for doctors to help those who are sick.
3. It provides me with a way to help people

The most popular responses for why you support CMRI:

25% It’s the only children’s medical research institute in Australia that focuses on genetic research
27% The majority of of my donation goes directly towards children’s medical research
21% I know that CMRI is founded with and relies on community support from people like me
43% CMRI’s track record proves my donation is used to create the building blocks for future medical treatments

The areas of research you are most interested in:

Cancer 63% Neuroscience 8%
Gene Therapy 21% Embryology 8%
Professor Phil Robinson was awarded a highly competitive National Health and Medical Research Council Senior Principal Research Fellowship for the fifth consecutive time based on his work developing new treatments for epilepsy and the ProCan project for cancer research, diagnosis, and treatment planning. He was also awarded the third largest Australian Research Council (ARC) grant in Australia.

Professor Roger Reddel’s outstanding contributions in the field of medicine were recognised with The Neil Hamilton Fairley Medal for 2017. The Royal Australasian College of Physicians (RACP) awards the medal only once every five years, and Prof Reddel was recognized for his outstanding contributions to telomere and cancer research.

Professor Ian Alexander received a highly competitive NHMRC Project Grant for his gene therapy work.

Professor Robyn Jamieson’s work on inherited blindness was included in Sydney University’s Research Excellence Initiative 2020, to help Sydney researchers test new ideas and push disciplinary boundaries.

CMRI’s Deputy Director Patrick Tam received a Distinguished Professorial Achievement Award at the University of Sydney’s Faculty of Medicine annual dinner in April. Patrick was honoured for his outstanding career achievements in embryology research and “extraordinarily diligent and committed service to the scientific community”.

Professor Roger Reddel’s outstanding contributions in the field of medicine were recognised with The Neil Hamilton Fairley Medal for 2017. The Royal Australasian College of Physicians (RACP) awards the medal only once every five years, and Prof Reddel was recognized for his outstanding contributions to telomere and cancer research.
Thousands of fellow supporters around Australia have joined you in supporting Children’s Medical Research Institute by participating in events like Jeans for Genes Day and the Great Cycle Challenge.

During October, 11,136 Great Cycle Challenge riders pedaled a total of 2,224,590 km and raised an impressive $3.18m for our work at CMRI.

There have been many inspiring stories along the way. Dozens of riders decided that, rather than racing in their own name, they would form a collective team raising money in the name of young Levi who is fighting cancer. Levi’s Legends included the number one fundraiser nationally – Warren Floyd – who personally raised $26,558.

Another particularly impressive result came from 10-year-old Imogen Kuipers who rode 600km and raised $10,000. She has even been chosen to take part in the Queen’s Baton Relay for the Commonwealth Games, in recognition of fundraising efforts over the years for CMRI. All up, she has raised more than $30,000 doing the Great Cycle Challenge.

The best part of this year’s Great Cycle Challenge was hearing that one of our shining stars, little Brody, who has been doing his best to “kick cancer’s butt” has done it. During the final days of the campaign, he got test results to show that he is officially cancer free!

That’s what it’s all about.

If you ask seven-year-old Maddy Luk what she wants to be when she grows up, she’ll answer without hesitation – “a teacher, because I love to tell people what to do” and burst into hysterical giggles.

“She tells everyone that, all the time,” mum, Nicole Luk, laughs.

Maddy was a 2017 ambassador for Jeans for Genes, and the family are supporting us again in 2018 for our 25th Anniversary year.

“My kids are happy and in many ways just normal kids. That said, I do believe more research needs to be done into ways to improve their quality of life,” Nicole said.

Both Maddy and sister, Briella, have diastrophic dysplasia, a genetic disease. They were born with a cleft palate, have difficulty breathing due to the size of their ribs, and have developed kyphoscoliosis, a deformation of the spine.

In the first half of 2018, they will undergo spinal surgery on the same day. They will then be put in traction for a couple of months to straighten their spines. And further surgery may be needed.

“I believe [this genetic disease] has made us all more accepting and understanding. Life isn’t fair and we all just need to play the hand we are dealt,” Nicole said.

The Luk family feel very lucky and want to do whatever they can to educate others about the importance of medical research.

At part of the 25th anniversary of Jeans for Genes, Children’s Medical Research Institute aims to raise $25 million for a new centre of collaboration, which will bring together research and hospitals to better help Australians kids affected by genetic diseases.

You can join Maddy in her fight against genetic disease, and you don’t need to wait until Jeans for Genes Day on August 3rd to start fundraising.

Please sign up now to fundraise, volunteer, or donate at jeansforgenes.org.au

Jeans for Genes®

Jeans for Genes and Great Cycle Challenge – Events that Bring People Together
Committee and Community Support Highlights

There is nothing more valuable to CMRI than its committees, who are the lifeblood of our fundraising, and in 2017, they went from strength to strength. The year kicked off with the Quirindi Committee holding its 50th Anniversary Black Tie Gala and raising an incredible $100,000! Committee President, Amanda Murray, said even they were surprised by the amount. “The community response was absolutely overwhelming.”

The Hills Committee is known for their spectacular Mother’s Day Luncheon, held at the Hilton Hotel. The 2017 event featured talks from guest speakers Ita Buttrose and John Mangos and raised $50,000. They also paid very special tribute to Jenny Gilbert from the Committee, who recently passed away.

Our newest fundraising committee is the Cessnock City Supporters Group, but the members have been fundraising for CMRI for many years through the Quota and Rotary clubs. In October, the members presented a $10,000 donation and visited CMRI at Westmead to see what the results of their hard work would be used for.

Another highlight of the event calendar is the Strathfield Committee’s Quiz Night, which had a “Friday the 13th” theme. More than 120 people attended and helped to raise $6,000 – adding to the $1.7 million total achieved over their impressive 33-year history.

At Gerringong, the 27th Annual Quilt and Craft Show in November showed why it is still going strong. The committee raised $19,000, thanks to the support of the Illawarra community.

When Christmas approaches, you can count on some pretty impressive CMRI fundraising committee events. One is the Wagga Committee Christmas Fair. Wagga celebrated their 30th birthday by raising $50,000 – an impressive amount, which they manage every year. The final event for 2017 was the Canberra Committee’s incredible Annual Luncheon, which raised $30,000. Always held in a spectacular location, this year it could be found at historic Merryville Homestead in Yass, thanks to hosts Ning and Robert Clark.

CMRI congratulates each member of these and other hard-working committees. Thank you for your dedication and the difference you are making for the future of children everywhere.

The 30th Birthday Party for one of our most dedicated corporate fundraisers, Stanford Brown Financial Advisers, was a huge success.

More than 480 people gathered to mark the anniversary of the business, which started just one day before the Great Stock Market Crash of 1987, and has gone on to thrive.

Stanford Brown has had a relationship with CMRI for many years. As part of their birthday activities, Stanford Brown decided to use their ball as a fundraiser.

CMRI’s Dr. Tony Cesare, Head of the Genome Integrity Unit, spoke about the research he and his team are undertaking. The entire Genome Integrity Unit and several other members of CMRI and its Board attended or donated their time.

It was a terrific celebration and we thank founder, David Brown, the Stanford Brown Board, staff and clients for their generosity in support of CMRI on the night.

Honour Roll

Children’s Medical Research Institute unveiled a unique piece of artwork outside the Institute in Westmead in October. This Honour Roll Wall was built to thank some of the people who help to make our work possible.

The design encompasses feng shui principles and includes 10 rainbow-coloured, helix-shaped structures, which resemble a DNA strand. Each helix includes gold, silver, and bronze plaques with the names of 79 generous donors and space for more in future.
Other ways to get involved:

You can help us defeat childhood genetic diseases. Here are some ways you can be a supporter of the team at CMRI:

- **Become a GameChanger:** when you sign-up as a regular donor, you join our team as a GameChanger - a special group of CMRI supporters whose generosity and foresight are ensuring a brighter future for Australian children.
- **Ensure your legacy lives on** through research by leaving a gift in your Will.
- **Become a Jeans for Genes® Genie:** sell merchandise or organise a fundraising event, any time of year.
- **Challenge events:** Run, ride, swim or take on a team challenge. Run in the City-To-Surf or other events to raise money for CMRI’s vital work.
- **Great Cycle Challenge™:** Get a team together, set a riding target and fundraising goal and use our online platform to track your progress. Ask colleagues and friends to sponsor your team as you ride throughout October.
- **Join us at our annual Jeans for Genes Denim Dinner,** or come along to another function. Visit cmri.org.au/events
- **Purchase Christmas cards and gifts** from our online shop at shop.cmri.org.au
- **Volunteer:** Help behind the scenes at events or talk to us about other volunteering opportunities.

**Discovery Day**

Ever wondered what a research laboratory looks like? You are invited to see CMRI’s work first hand by visiting the Institute, and hearing more about our research and watching scientists at work.

If you would like to attend a Discovery Day contact us on 1800 436 437 or email info@cmri.org.au to make a booking.

Visit our website cmri.org.au or contact us on 1800 436 437 to learn more.

Again, a huge thank you to our generous donors, and we look forward to even more successes in 2018. Together, we will find cures for children’s genetic diseases.
Finding cures for childhood genetic diseases

Children’s Medical Research Institute:
postal: Locked Bag 2023, Wentworthville NSW 2145 Australia
ABN 47 002 684 737 Freecall: 1800 436 437
Email: info@cmri.org.au
cmri.org.au | jeansforgenes.org.au