Under the microscope

CHILDREN'S MEDICAL RESEARCH INSTITUTE

NEWS FROM INSIDE THE INSTITUTE FOR OUR SUPPORTERS

SUMMER EDITION **2015**

Your support helped us more than ever in 2014

With NHMRC grants announced in October last year having only a 1 in 7 success rate across Australia, the support you give us is increasingly vital.

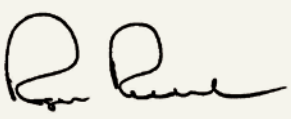
During the Spring mailing last year, you raised over a staggering $100,000! This is going towards my team in the Cell Cycle Unit who are making exciting progress on one of the worst cancers affecting young children – brain tumours. Our discoveries show that we are targeting the right proteins to shrink brain tumours in the laboratory, but for the next steps we need funding which you have generously contributed to, to create suitable compounds to test this research for human use.

Sadly, the cure rate of advanced brain tumours has improved little over time, and only 10-30% of patients survive two years after their diagnosis. With your support, our goal is to find more effective treatments that will save more precious young lives. Thank you for the impact you are making.

Healthier kids, brighter futures

Sharing discoveries with our supporters is one of the things I enjoy most, and I'm sure you will be very interested to hear about three major discoveries that have been made since our last newsletter. One of them is about the role of the Otx2 gene in head and brain development and in birth defects. This work was conducted by Dr Nicolas Fossat who is featured in this issue. Also featured in this issue is Associate Professor Tracy Bryan's work on a gene (TPP1) responsible for inherited bone marrow failure. This knowledge will help researchers around the world better understand bone marrow failure, as well as cancer. People, like Diandra Edmondson, with this genetic disease face many difficulties, and Diandra shares her story with us. Finally, another tremendous achievement for our cancer research programs is the work led by Dr Hilda Pickett on ALT (Alternative Lengthening of Telomeres) cancers. These include some of the most aggressive types, such as glioblastoma brain tumours, and the findings are our greatest single advance in understanding the molecular details of ALT since it was first discovered in our institute 20 years ago. I hope you enjoy this edition of Under the Microscope, and please visit the news section of our website for more details on all of these stories and more (www.cmri.org.au/News/Latest-News).

Best wishes for the year ahead,



Professor Roger Reddel

Congratulations to Omesha Perera on winning the 2014 Star Alliance Travel Scholarship. Omesha is in her final year of her PhD in the Cell Biology Unit at CMRI. This invaluable scholarship allowed Omesha to attend the EMBO conference in Belgium, exchanging vital knowledge with international researchers in this field.

STAR ALLIANCE
THE WAY THE EARTH CONNECTS

Gene discovery offers hope for aplastic anaemia and cancer

Researchers from Australia, the USA and China identified a mutation they thought could be causing aplastic anaemia, but they needed CMRI's Associate Professor Tracy Bryan to find out for certain.

Associate Professor Tracy Bryan, Head of the Cell Biology Unit at CMRI and an international expert on telomerase, spearheaded the research.

TPP1 is a gene needed for the normal functioning of telomeres, which are the caps on the ends of chromosomes that shorten as we age.

Associate Professor Tracy Bryan's group discovered that the inherited defect in TPP1 prevents an enzyme called telomerase – which keeps telomeres from shortening too much – from accessing telomeres.

This means that patients with this defect have very short telomeres in cells throughout their body, and are more susceptible to bone marrow failure.

"The TPP1 gene is one our lab specialises in," said Associate Professor Tracy Bryan, "and we have the technology required to show that the mutation found in the family causes short telomeres. This is now the 10th gene identified that causes short telomere syndromes. These syndromes manifest as a predisposition to certain blood disorders and cancer, and failure of organs such as the lungs and liver. Aplastic anaemia, a severe blood disorder caused by bone marrow failure, is the disease caused by this particular mutation in TPP1."

By showing that the defect in TPP1 causes this disease, Tracy hopes doctors around the world will be able to more easily identify patients that are predisposed to aplastic anaemia. This discovery will also assist future research aimed at finding treatments for short telomere syndromes and cancer.

The research involved a collaboration between CMRI, The Children's Hospital at Westmead, the Children's Hospital of Philadelphia (USA), and BGI-Shenzhen (China).

"What we have discovered is not only a huge step forward for short telomere syndromes, but it also adds to our understanding of the role of telomerase in cancer and ageing," said Associate Professor Tracy Bryan.

— For more information and to watch a video from NBN News, visit www.cmri.org.au/News/Videos

Our 2014 Great Cycle Challenge raised over $2.1 million. A massive thank you to all 6,800 participants from around Australia who rode and raised funds for CMRI's cancer research units.

Congrats to CMRI's young researchers Alan Ma, Masters student (Best Oral presentation) and Rebecca Greenlees, PhD student (Best Poster Presentation) – the winners of Westmead Hub Research week presentations. Encouraging signs for the research stars of the future!

You sent us your wonderful messages of hope in response to our Christmas Appeal mailing and brightened up the Institute – thank you!

Just like the cancers, birth defects and genetic diseases they study, our researchers are not bound by borders. Children's Medical Research Institute's Dr Nicolas Fossat, originally from France, joined the Embryology Unit seven years ago. He takes us through what his work aims to achieve.

Q & A

With Dr Nicolas Fossat

Q: Why did you move from France to work at CMRI?

A: I really wanted the opportunity to establish myself somewhere else in the world. When I looked into opportunities in Sydney I learned Patrick (Tam) worked at CMRI and I was very familiar with his work, because he is very well known in the world. I really wanted to train with and learn from him, so I contacted him and was fortunate enough to get a position at CMRI in 2007. I've been here ever since.

Q: Tell us about the Otx2 gene you've been working on.

A: I have been working on the Otx2 gene since my PhD studies. It's a gene that's really important for the formation of the head and the brain. When the Otx2 gene is missing, an embryo develops without a head. If you don't have this gene in a human baby it means it will unfortunately die during gestation. We know a percentage of babies are likely to die before they reach three months after conception, and we think it's possible that a mutation in the Oxt2 gene that completely inactivates it could be one of the causes of this. But we also know that there are some mutations in Oxt2 that do not inactivate it fully, and these result in children being born with eyes that aren't properly formed, or with problems in the formation of parts of the brain. Loss of Otx2 gene function in an adult can cause blindness because some types of eye cells die as a result. I'm still investigating Otx2, still working on it, but it's in the very early stages of development and I'm focusing particularly on the formation of the head. What I'm finding has very important implications for children, which is very exciting indeed.

— To ask one of CMRI's scientists a question send an email to marcomms@cmri.org.au

Committee & Community news

With CMRI committees & supporters

Hills Committee High Tea and Fair
The sun shone on the grand variety of stalls in the glorious gardens of Curzon Hall in October last year and guests mingled amongst them before having a grand High Tea with Maria Venuti as the talented MC. Thank you to Patti Payne and her committee for organising such a beautiful event.

Gerringong Committee
The Annual Quilt Show arranged by the Gerringong Committee raised over $18,000 for CMRI. The most amazing quilts were on show (and some for purchase) at the Gerringong Town Hall on the first weekend in November last year.

Canberra Committee Luncheon
The Canberra Committee Luncheon, hosted by Mr Rob Purves and Ms Bronwyn Darlington, was attended by 460 guests in Spring last year. Guests browsed the stalls and enjoyed a delicious picnic lunch at the "Carwoola Station" property.

Wagga Wagga Fair
Wagga Wagga Committee's 2014 CMRI Christmas Fair in October last year saw over 3,500 attendees and 98 stalls raise well over the target of $49,000.

The Wagga Wagga Fair was a wonderful success.
— For the full story, go online.

Dates for your diary

17/02 & 17/03 CMRI Discovery Days – come and learn about the important work being done at CMRI

21/03 50th Birthday for Port Hacking Committee at Cronulla Golf Club – 7pm, $150

08/05 Hills Committee Mother's Luncheon

18/11 2015 Canberra luncheon at Lambrigg Station

— Contact Jennifer Philps (jphilps@cmri.org.au) for more information on upcoming events, or visit cmri.org.au/events.

Diandra's story

Associate Professor Tracy Bryan's research at CMRI has recently demonstrated that one mutation in a gene called TPP1 caused Diandra Edmondson's disease. This is Diandra's story:

"I was eight years old when I was diagnosed with aplastic anaemia. I didn't know how serious it was, and it has gotten much worse over time. I now realise the severity of it.

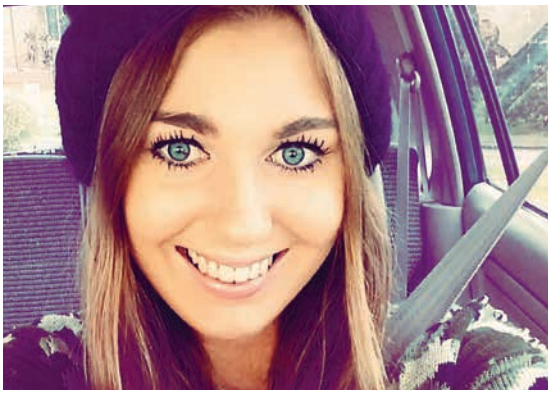
"Treatment put me in hospital during every school holiday. It's harder to deal with now that I'm 19 – I'm at an age where I want to do things and I can't do them.

"I had a bone marrow transplant in November last year because blood transfusions were keeping me alive, and they weren't going to work for much longer. There's no medication I could have taken.

"I think research will be good to one day develop medication that could help blood and platelet levels come back up on their own. It's going to take a lot of research and a lot of time and that's why CMRI's work is so important.

"My advice for kids newly diagnosed with a rare disease is to get educated about your condition. It's better if you know about your condition or your gene.

"In terms of living with it, everyone is different, but I don't think too far ahead. With a gene problem you don't know what's in the future – I didn't know I'd need a bone marrow transplant. Otherwise, you get disappointed when you can't do what you want to do. The best thing I've ever done is learn everything I possibly could about my aplastic anaemia.



"I think research will be good to one day develop medication that could help blood and platelet levels come back up on their own. It's going to take a lot of research and a lot of time and that's why CMRI's work is so important."

"I know what can go wrong, what to do, and what not to do. After my bone marrow transplant, I was in a locked ward to protect my immune system. I could go out with a face mask but I knew the risks of infection and I didn't want to take that chance. My main focus was getting to leave hospital and go home.

"After that? I'm not able to do anything for 6-12 months while I'm recovering from the transplant, so it's hard to make plans. I do want to go to TAFE, get a job… I want to go on holiday. Since I was eight, I've been in hospital two to three times per week, so it's impossible to go away. I really want to go on holiday one day."

We at CMRI think Diandra definitely deserves a break, so we wish her all the best for her recovery and will continue working towards better treatments and cures for conditions like hers.

Be a part of history by making a donation today and helping to fight childhood disease

Please accept my gift of: ☐ $30 ☐ $45 ☐ My own choice of $ DC115

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☐ Please send me more information about including a bequest to Children's Medical Research Institute in my Will

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☐ *We occasionally invite other like-minded organisations to contact our supporters. If you prefer not to receive such communications please tick the box.*

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www.cmri.org.au/donate

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