

under the microscope



Features

Understanding Telomerase	2
Muscle Weakness Diseases	3
Jeans for Genes	4
Embryo Development	5
Dates for your Diary	6

Today's scientists for tomorrow's children

The Children's Medical Research Institute (CMRI) is an independent organisation committed to unlocking the mysteries of disease. Our scientists investigate conditions such as birth defects, cancer, and epilepsy. Our philosophy is that major advances in prevention and treatment come from research into the fundamental processes of life. Our work is made possible by our community of supporters and Jeans for Genes®.

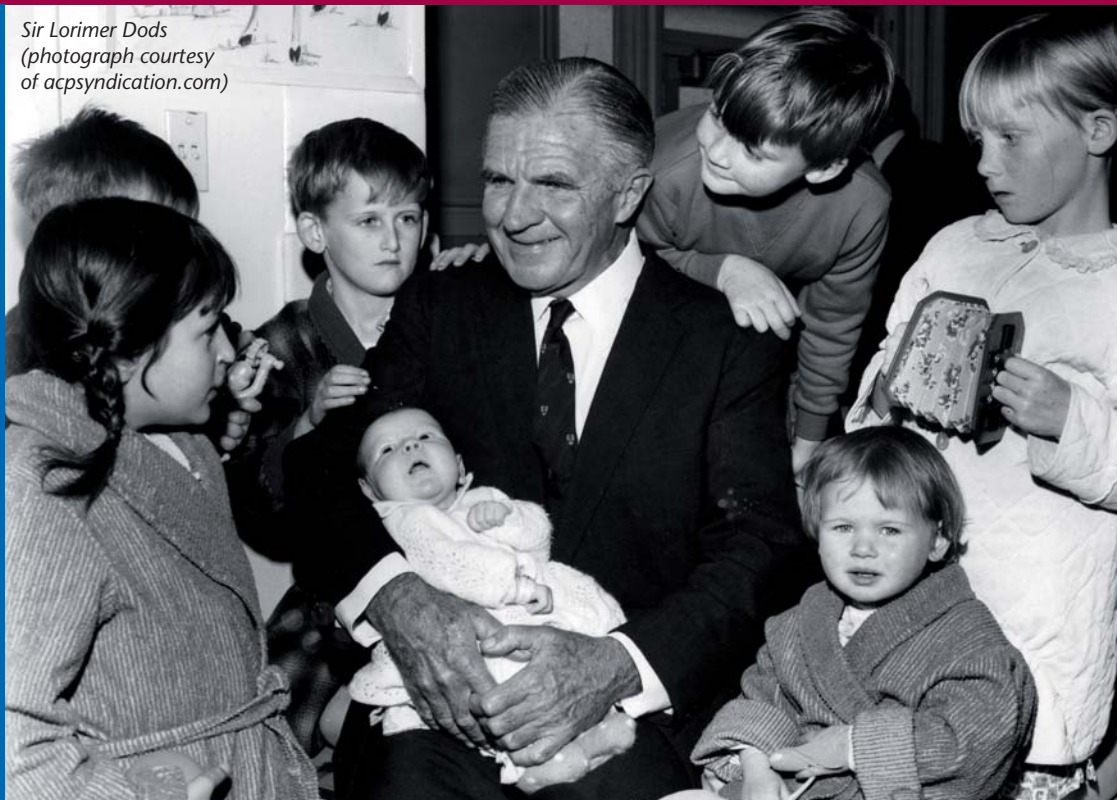
50 YEARS OF
DISCOVERY
CHILDREN'S MEDICAL RESEARCH INSTITUTE

Produced by the Fundraising & Community Relations Department, Children's Medical Research Institute

Locked Bag 23
Wentworthville NSW 2145
Tel 02 9687 2800
Fax 02 9687 2120
Freecall 1800 GENIES (436 437)
Email info@cmri.com.au
Website www.cmri.com.au

© CMRI 2008

Sir Lorimer Dods
(photograph courtesy
of acpsyndication.com)



Celebrating 50 Years of Discovery

In 1958 the Children's Medical Research Foundation (CMRF) was established by the Royal Alexandra Hospital for Children at Camperdown, with funds raised by a large public campaign – including one of Australia's first telethons. The foundation is now independent and called the Children's Medical Research Institute (CMRI). Although the name has changed the philosophy and vision of founder and honorary director of the Institute, Sir Lorimer Dods, still holds true.

"The object of such a unit would include studies of the nature and causation of the many diseases and disorders of infancy and childhood, the development of new methods of diagnosis and of treatment (both medical and surgical), and research into the most important problem of all – prevention..." Sir Lorimer Dods

Fifty years on, CMRI scientists have made major advances – reducing the incidence of congenital rubella, improving newborn survival, and repairing obstructions to the bowels of tiny babies – to name a few. With more recent laboratory-based research, our scientists are now unravelling the causes of conditions such as cancer, epilepsy and birth defects as they strive to develop new treatments for the future.

As CMRI commemorates five decades of groundbreaking research, the Institute is hosting a number of exciting 50th anniversary events. For details please see dates for your diary (page 6) or visit www.cmri.com.au

Director's desk



In 2008 we are celebrating CMRI's 50th year of paediatric research, and will be holding a number of special events to mark this milestone in our history. During this time there have been remarkable improvements in children's health, to which CMRI has been a proud contributor. But there are still many unsolved problems of children's diseases that result in ill-health, disability and premature death. I am sure that the founders of CMRI would be amazed and delighted by the power of the research technologies that we currently have at our disposal, and the excellence of the research team that has been assembled. With these wonderful capabilities comes the responsibility of using them in the most effective way.

As we look to the future, the CMRI team remains fully committed to the simple but powerful principle that guides all that we do - a conviction that the major advances in child health will come from fundamental insights into the normal processes of life, and what goes wrong in disease. This requires painstaking work, persistence and long-term commitment, in the expectation that the rewards will be priceless.

We look forward to the challenges of the next 50 years. With your help, we will continue to make a difference.

Happy New Year and Happy 50th!

Professor Roger Reddel

Teaming up to Understand Telomerase

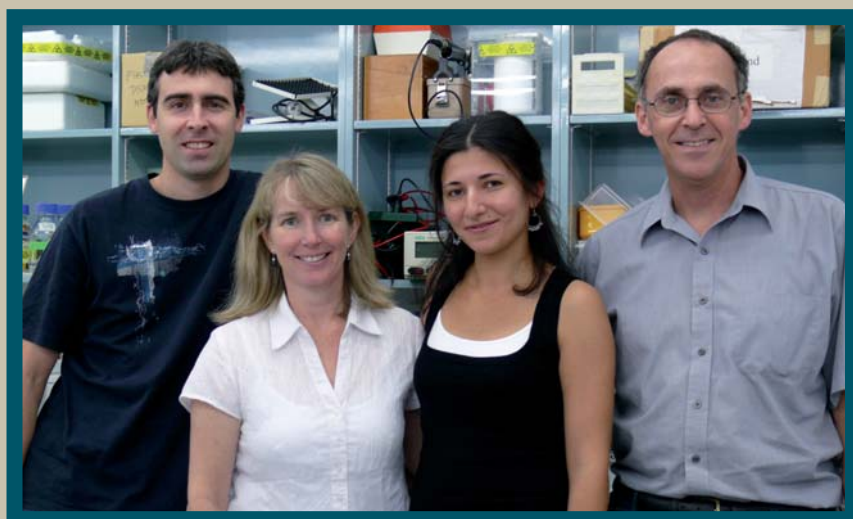
The enzyme telomerase is found in at least 85% of tumours, and it is exciting that teamwork between scientists in CMRI's Cell Biology Unit (CBU) and Cell Signalling Unit (CSU) is now leading to a better understanding of how this protein functions. This kind of information is essential as researchers attempt to develop more targeted and safer cancer therapies.

Researchers already know that the DNA at the end of each chromosome, called the telomere, normally gets shorter as cells multiply, until it becomes so short that cells stop multiplying altogether. Most cancer cells use telomerase to extend the length of this DNA, allowing the cells to multiply without limit. A complicating factor, however, is that the DNA at the very end of the telomere can fold into different shapes, potentially changing its interaction with telomerase.

Scientists used to believe that telomerase could only extend the simple unfolded form of telomere DNA. So drugs were designed to lock DNA at the end of all chromosomes into the more complicated folded structures, to block telomerase activity and stop cancer cell growth.

In 2006, however, CBU's Liana Ogenesian found that this line of drug development may be misdirected. She showed that telomerase can extend a more complicated form of telomere DNA after all (UTM Winter 2006). At the time, Liana could only make an educated guess about the exact structure of this DNA, but CSU's Dr Mark Graham has now confirmed that this was correct using CMRI's mass spectrometer.

Recently, Liana discovered that when telomerase is artificially altered in a specific way it interacts differently with folded and unfolded forms of DNA. This gave her the first clues that a portion of the telomerase molecule needs to undergo a change in its shape to deal with folded DNA. "This knowledge will aid the design of better anti-cancer treatments in the future," says Associate Professor Tracy Bryan, Head of the CBU.



Drs Mark Graham, Tracy Bryan, Liana Ogenesian and Phil Robinson

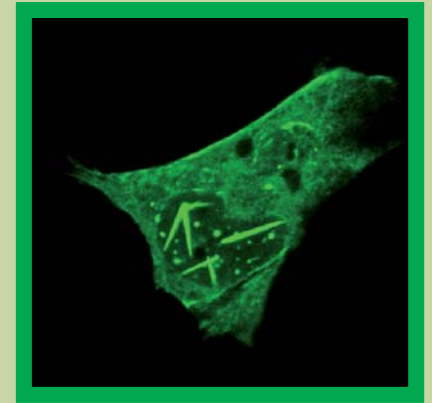
Muscling in on Muscle Weakness Diseases

Exciting progress has now been made by researchers from CMRI and The Children's Hospital at Westmead (CHW), who have made a number of important new discoveries about two muscle disorders. Understanding the root cause of these serious conditions is important, as inherited muscle disorders often lead to debilitating muscle weakness, which can be fatal.

Researchers at CHW were studying a family with Intranuclear Rod Myopathy, a condition in which muscle weakness is caused by abnormalities in a protein called actin. To measure the altered protein, Val Valova, who runs CMRI's mass spectrometry facility, developed a special test. She found abnormal levels in three affected family members.

CHW's Dr Ana Domazetovska discovered that this altered protein can interfere with the function of other muscle proteins and parts of the cell's inner machinery. In addition, the joint team also found that rod-like structures* – which are a feature of this type of muscle disease – adversely affect the function of a cell. The effects could contribute to muscle weakness in patients.

CHW's Nigel Clarke and CMRI's Val Valova have also studied children with another muscle weakness disorder, called Congenital Fibre Type Disproportion, and found that different alterations in the same muscle protein (actin) can also disrupt the way muscles generate force when they contract.



**A 'rod-like' structure in a muscle cell (photo courtesy of Ana Domazetovska)*

CMRI Unit Heads, Professor Phil Robinson and Associate Professor Edna Hardeman, and Professor Kathryn North, Head of the Neurogenetics Research Unit at CHW, agree that teamwork has been important in understanding how different types of changes in just one protein can cause distinct muscle disorders. The work of the CMRI and CHW researchers has led to new discoveries and lays the foundations for developing treatments for children with these disabling and potentially lethal disorders.

Immune Boost

Solid tumours are difficult to treat as cancer cells deep in the tumour are hard to reach with usual drug delivery methods. Many patients also do not generate sufficient immune cells to help fight the cancer.

Dr Priya Ganesan* has now programmed immune cells to 'search and destroy' tumour cells. Priya isolated immune T cells from a mouse with cancer and encouraged cell division in the laboratory to increase T cell numbers. She then stimulated them using tumour cells with a molecular tag on the cell surface – a protein known to promote immune cell production.



Dr Priya Ganesan

After re-introducing the immune cells into the mouse, she demonstrated that this molecular tag boosts immunity against the cancer cells and that the immune system develops a memory of the tumour cells – generating a more vigorous response to subsequent tumour challenge.

**This recently published report was completed as part of Priya's PhD thesis in the Gene Therapy Research Unit – a joint initiative between The Children's Hospital at Westmead and CMRI.*

NEWS

Professor Roger Reddel has been awarded the title of **Lorimer Dods Professor** by the University of Sydney. This title has been conferred to the Director of the CMRI since 1980, to commemorate the vision and passion of founding father Sir Lorimer Dods.

Four prestigious **Cancer Institute of NSW research grants** have just been awarded to CMRI scientists, Drs Daniel Speidel, Megan Fabbro, Amy Au and Associate Professor Tracy Bryan, to study molecules involved in cancer development and to design better cancer therapies for the future. Dr Nicolas Fossat of the Embryology Unit has also been awarded a highly competitive **University of Sydney Post-doctoral Research Fellowship** for research into the early development of the embryonic gut.

Myopia or Near-Sightedness affects approximately one third of Australians, and unravelling how this comes about could lead to a better understanding of this common ailment. Now CMRI's Dr Robyn Jamieson and eye researchers from Adelaide, Melbourne, Tasmania and Edinburgh have worked together to show Australian patients who inherit errors in a gene called PAX6 also have a tendency to develop near-sightedness.

Jeans for Genes®

Christmas Gift Wrap for a Cause

Thanks to the support of over 350 Genies, \$33,382 was raised in the 'Jeans for Genes Gift Wrap for a Cause' program – run in conjunction with Myer and Rhodes Shopping Centres. From CDs to DVDs, massage machines to coffee machines, our Genies turned simple items into beautiful gifts. Valentine's Day gift wrapping took place at selected Myer stores on February 13 and 14.

A.S.K Solutions Christmas Party raises \$29,000 for Jeans for Genes

For the first time, ASK Solutions kindly chose Jeans for Genes and CMRI as their charity of choice for their end of year Christmas party, which was held at Star City. Fun was had by all with raffles, a great live auction, magic show and trivia. The team at Jeans for Genes were very thankful to receive such fabulous support.

Gift-matching Gene-erosity

The First Data International North Sydney office once again raised money for Jeans for Genes, and this amount was generously increased as part of a gift-matching scheme by their Head Office in America.

Events 2008

Do it with Denim® – Australia's next top designer competition

Know someone with style and flair that would like to be Australia's next top designer of fashion or furniture? Go to doitwithdenim.org.au for information on how to enter.

Jeans on the Green Golf Day – Friday May 23

Take part in this unique and fun event. Put together a team of four and have loads of fun at Oatlands Golf Course. For further details, please contact Christine McGee on 02 9687 2800 or cmcgee@jeansforgenes.org.au

Toyota Financial Services proud to support Jeans for Genes and the Denim Gold Charity Dinner – July

To help celebrate CMRI's 50th anniversary, Jeans for Genes is holding an exclusive Denim Gold Charity Dinner and Toyota Financial Services (TFS) is once again proud to support Jeans for Genes and in particular the Charity Dinner.

"TFS's major contribution this year of \$30,000 will make a very significant difference," says Julijana Trifunovic, National Campaign Manager for Jeans for Genes. "And since TFS staff also sells merchandise on Jeans for Genes Day and charity gift wrap - we are working together to find cures in more ways than one."

Jeans for Genes rely heavily on the goodwill and generosity of companies such as TFS and their commitment to our research. If you or your company would like to get involved, please contact Christine McGee on 02 9687 2800 or cmcgee@jeansforgenes.org.au

Take part in a Mass Denimstration on Jeans for Genes Day Friday August 1

Plans are underway for another successful Jeans for Genes Day. And to celebrate, "50 years of discovery" at the CMRI, Jeans for Genes will issue a fabulous selection of merchandise, including a commemorative \$5 gold badge with diamante and for only \$10 a special edition Grant Hackett jeans badge (see photo). We will also be launching a number of exciting partnerships during the year. We hope you too will take part in the 15th year of this great event, which has raised over \$41 million for the CMRI.

Jeans for Genes is a major fundraiser of the Children's Medical Research Institute



Julijana Trifunovic receiving a huge cheque from Ian Ritchens, a driving force behind TFS support



TTA staff got behind 'Gift Wrap for a Cause'



Grant Hackett Jeans Badge



A.S.K Solutions Group Christmas party



Do it with Denim 2007 finalists and national winner (second from right)



Committee Power

COMMITTEES

On a glorious spring day over 400 guests were privileged to enjoy the beautiful garden at 'Redbrow', Murrumbateman, the venue for the 2007 **Canberra Committee Luncheon**. The rains ensured the garden looked its best and wines were generously donated by Pernod Ricard Pacific (Jacob's Creek Wines).

Racquet Committee's Christmas Pantomime 'Puss in Thongs' by the Pymble Players was a very entertaining fundraiser. Thank you to the Pymble Players, who also celebrate their 50th anniversary this year!

Many thanks go to members of CMRI's **Gosford Committee**, who have purchased a special safety cabinet for scientists to use when dispensing cancer drugs. These drugs are being used to test exciting new approaches for the treatment of paediatric cancer or muscle weakness disease.

A warm welcome to the new **Coffs Harbour Committee**, formed in our 50th anniversary year by a group of dedicated and enthusiastic supporters. We look forward to sharing your news and ideas into the future.

OTHER SUPPORTERS

Queensland supporter **Foster Lee** has just produced a CD, "A Tribute to Legends", and he has generously offered to donate 30% from each sale to CMRI, please visit www.foscyninvestments.com

On a wet November weekend the annual **Treasury of Craft Fair** at the Don Moore Community Centre brought much Christmas Cheer to North Rocks - to raise funds for CMRI.

We are grateful to the **Catenian Association Castle Hill Circle** who generously made a donation towards CMRI research and thanks also go to **Professional Trial Papers** for their generous support.

A successful **"Moving Art" Exhibition** was held at the Weswal Gallery, Tamworth this January. Opened by country and western singer Lonnie Lee the first CMRI 50th anniversary event of the year was enjoyed by the invited guests.

Left to right:

President Bev Reynolds, Organiser Roz Onorato and chocolate maker Alfina Sfirse of the Treasury of Craft Group;

Trish Donovan (Moving Art Organiser), Lonnie Lee and Verity Bligh (President Tamworth Committee);

Cathy Johnston of Pernod Ricard Pacific with Canberra Committee President Celia McKew;

Coffs Harbour Committee's Stacey Fagan, Tracy Heading, Sophie Williams, Christine Harding and Rachel Howell and some of their children.

Dates for your Diary

Wednesday 12 March – Sunday 4 May: Visit CMRI's fascinating 50th anniversary exhibition, "50 Years of Discovery", at the National Museum of Australia, Canberra and discover for yourself the pioneering research of one of Australia's major research institutes – research which led to dramatically improved survival rates for premature babies, new vaccination programs, microsurgery and more. And see how current research may lead to new treatments for cancer and epilepsy in the future.

Sunday 16 March: Thumbelina Committee's **Hat and Fashion Parade** at 'Laurelbank', Willoughby in Sydney at 2pm. Contact Kathleen Stokes-McKeon 02 9416 2413.

Monday 6 May: Northern Beaches Committee will hold a **Charity Ladies Golf Day** at Mona Vale Golf Club, Sydney. Contact Maureen Botha 0402 021 739.

Friday 9 May: Hills Committee's **50th Anniversary Mother's Day Luncheon**, with mystery guest and fabulous MC John Mangos, will be held at the Hilton Hotel, Sydney. Contact Patti Payne 0418 867 784.

Wednesday 28 May: Beecroft Committee are holding a **Mixed Card Day** at Castle Pines Village in Sydney. Contact Mary Howell 02 8850 1271.

Saturday 31 May: Don't miss out on **Australia's Best Magician Show** at Glen Street Theatre, Belrose in Sydney, organised by the Thumbelina Committee. Contact John Seckold 0419 274 587 for details of the afternoon and evening show.

Wednesday 4 June: Vaucluse Committee's theatre party **'Phantom of the Opera'** at the Lyric Theatre, Sydney. Contact Jan Madigan 02 9345 4331 (limited seats).

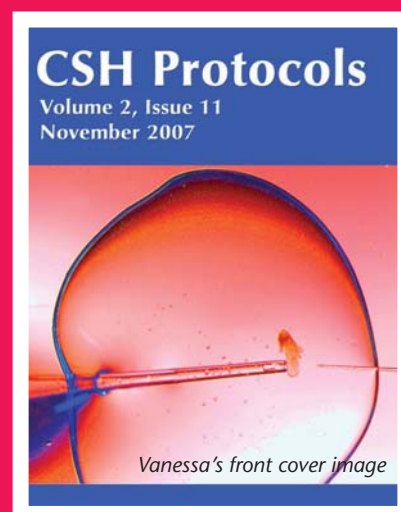
Friday 13 June: Celebrate at Strathfield Committee's **Golden Anniversary Gala Dinner** at 'La Mirage', Five Dock in Sydney. Contact Joyce Thiele 02 9363 3622.

Sharing New Technologies for Studying Embryo Development

Embryologists Heidi Bildsoe, Vanessa Franklin and Poh-Lynn Khoo are working with the tiniest of mouse embryos as they strive to unravel the fundamentals of how we develop. This research has led to the design and improvement of new technologies to visualise the earliest cell movements in living embryos – part of a process called fate mapping* – and these techniques have recently been published by the prestigious Cold Spring Harbor Laboratory (CSHL) Press.

In three articles, the CMRI scientists describe 'zapping cells', 'cell grafting' and 'embryonic cell painting' – methods for tracking fluorescently labelled cells. Vanessa's spectacular 'cell grafting' image features as a front cover of the journal *CSH Protocols*, and Heidi's method of cell painting to examine critical stages in early embryos is showcased as a feature article. "Having your papers highlighted in journals of the CSHL Press is an accolade that many scientists dream of but seldom receive," says Professor Patrick Tam, Head of the Embryology Unit. "It is a tribute to the quality of our work."

*For more details, see *UTM Winter 2007*.



Prevention is better than cure...

And the key to prevention lies in research.

It's as simple as that!

There are over 10,000 known genetic disorders. To correct these and many other disorders research is needed to find the causes.

Here is my gift:

\$200 \$100 \$50 \$25 Other \$

Please find enclosed my cheque

Please charge my credit card:

Mastercard Visa Amex Diners

credit card number

cardholder's name

cardholder's signature

expiry date

name

address

postcode

telephone

Please send me:

- More information about CMRI
- Christmas catalogue
- Information on my nearest fundraising committee
- An annual report
- Information on how to make a bequest
- Please update your records for my contact details

All donations are tax deductible



I would like to join the Automatic Credit Card Donor Program

Automatic Direct Debit Amount to be donated:

\$

Please complete the Credit Card Details at left.

Frequency: Monthly Quarterly Other

Commencement Month:

(processed first business day of month)

Please complete this coupon, enclose it with your donation in the envelope provided and mail to:

Children's Medical Research Institute
Locked Bag 23, Wentworthville NSW 2145 Australia
Tel 02 9687 2800 Fax 02 9687 2120

Thanks for your help.