

under the microscope

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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®.



**CHILDREN'S
MEDICAL
RESEARCH
INSTITUTE**

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*Little Gene-i-uses Charlie Breen and Wil Charters
Photo courtesy of Mark Taylor*

Gene-i-uses!

"The word of the day on
Jeans for Genes® Day"

A special **thank you** to all of our fabulous supporters, who raised much needed funds for the Children's Medical Research Institute (CMRI). Now in its fourteenth year, the campaign was as big if not bigger than previous years.

We had over 1000 volunteer 'Genies' out on the streets from 6.30am selling badges and groovy gear to commuters and shoppers in major cities throughout Australia. Many schools participated, with hundreds of children working together for a great cause. We also had many volunteers from companies as part of their philanthropic program, allowing staff to help out on the day.

Our regional supporters were just as generous with stories from far and wide about fabulous events in support of the day. There was a helix cake made for morning tea in Wagga Wagga, a swimathon in Narooma and many barbeques and 'Jamm for Genes®' gigs in over 100 towns and cities.

Continued page 4

Director's desk



I was recently privileged to attend the birthday party of one of the Children's Medical Research Institute's committees, who were celebrating 40 wonderful years of fundraising in the small and very sociable community of Quirindi – on the rich soils of the Liverpool Plains, southwest of Tamworth. Some of the original members of the committee were present, along with many other supporters, friends and family. Their ingenuity and hard work in raising money over so many years has been remarkable. It was quite obvious that working together for a cause has been a very enjoyable and gratifying experience for the whole team. But in addition to the enjoyment, I am convinced that this level of long-term commitment arises from a clear understanding that major medical advances are rarely, if ever, made overnight. The sort of research that has the greatest potential to make a difference to the lives of future generations usually requires extended periods of steady, patient work, interspersed with unexpected discoveries and flashes of insight. This is research that probes what makes healthy cells tick, and what can go wrong, yielding the knowledge that is essential for successful treatment and prevention of disease. We are very grateful to all of our supporters – new and old – who make this possible.

A handwritten signature in white ink on a blue background.

Roger Reddel
Acting Director

Sheepish Genes and Cystic Fibrosis

Three thousand Australians suffer from Cystic Fibrosis (CF), one of the most commonly inherited diseases in people of European descent. It is caused when there is a mistake in a gene important for the lungs to function properly, and unfortunately, although treatment for the condition has improved, CF patients still need constant therapy.

To improve treatment for this disease Dr Ian Alexander, Head of the Gene Therapy Research Unit*, and his team have been investigating the possibility of developing a gene therapy approach. This would involve delivering a healthy copy of the gene to the affected cells.

Developing a successful gene therapy strategy for cystic fibrosis is extremely challenging, mostly because of the architecture of the lungs. They are composed of layers of immature cells at the bottom and tightly-packed mature cells nearer the surface, at the interface between the air and the lungs. These mature cells are shed on a regular basis, so for a long-lasting treatment healthy genes need to be delivered to the immature cells and methods to achieve this have been elusive.

These gene therapy procedures have now been tested in sheep, which have a very similar pattern of lung development to humans. Using technically challenging surgical techniques, researcher Dr Jane Yu has managed to introduce a gene into the airways of foetal sheep in the womb. She used a modified virus to infect and deliver the gene to baby sheep lungs, whose mature cells are not properly formed at this stage of development.

Jane demonstrated that immature lung cells, especially in the more distant portions of the lung, are infected with the virus and that the gene which is delivered in this way is functional. These results are an important step in the right direction, towards a possible gene therapy approach for this disabling disease.

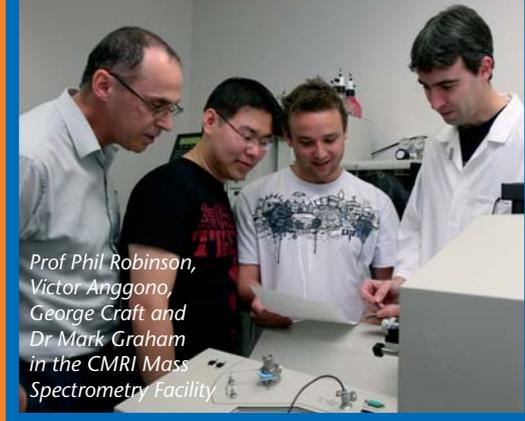
*The Gene Therapy Research Unit is a joint initiative between CMRI and The Children's Hospital at Westmead (CHW).

This work, published in the Journal of Gene Medicine, was undertaken in collaboration with the Department of Respiratory Medicine at CHW and sheep experts from the University of NSW and the Elizabeth Macarthur Agricultural Institute.

The 'O' on the front cover shows a section through part of a developing sheep airway in the lung.



Talking Neurons, CSI and Cancer



Prof Phil Robinson,
Victor Anggono,
George Craft and
Dr Mark Graham
in the CMRI Mass
Spectrometry Facility

What have wound age, brain cell communication and breast cancer got in common? Well the answer is, scientists in the CMRI's Cell Signalling Unit (CSU) have been studying all of these phenomena.

Sydney University forensic scientists Sarah Tarran and Neil Langlois enlisted the help of CMRI's George Craft and Valentina Valova to study wound age. Currently this is estimated by forensic pathologists who stain wound tissue and examine it under a microscope. The team discovered that proteins extracted from skin wounds at various times after they are inflicted can vary. For example, the level of haemoglobin changes within three hours. They are now searching for differences in proteins, rarer than haemoglobin, and present within a more precise time frame for use in forensic investigation.

So from CSI to unravelling the mysteries of brain cell communication, as CMRI's Victor Anggono continues to investigate the release and re-uptake of chemical messengers at nerve cell endings. Victor has already demonstrated that this process involves a novel interaction between two proteins dynamin I and syndapin I (spring 2006 newsletter). Recently he found that another protein endophilin I interacts with dynamin, at the same site as syndapin; although endophilin I interacts with only one site in this region whereas syndapin I interacts with two. It now appears that endophilin I might control recycling when there is a strong stimulus for lots of neurotransmitter release whereas syndapin I might be linked to slower release and recycling.

Lastly, CMRI's Mark Graham has teamed up with breast cancer researchers who are interested in Insulin-Like Growth Factor Binding Proteins (IGFBPs), as modification of these proteins has been linked to cancer. The scientists, from the Kolling Institute, wanted to look at different types of chemical modification (glycosylation and phosphorylation) of IGFBP-5 in breast cancer cells. Using a novel technique, which looks at both the whole protein and protein fragments, Mark was able to identify all sites of modification, thereby completing the analysis of the chemical composition of IGFBP-5. The next challenge will be to fully understand the effect of the phosphorylation on the function of IGFBP-5 circulating in blood.

"All of these projects relied on the capacity of CMRI's mass spectrometers to identify individual proteins or protein modifications," says Professor Phil Robinson, Head of the CSU. "This just goes to demonstrate the scope and the significant benefits of this new technology bringing together a diverse range of research disciplines."

NEWS SNIPS

CMRI's Data in Safe Storage. The CMRI now has a state-of-the-art computer Storage Area Network, which has greatly increased capacity, automated archiving, and the ability to take hourly 'snapshots' that improve data protection. Darryn Capes-Davis, Manager of CMRI's IT department, said "An improved storage system was essential to handle the large volumes of data from our new 'cell imaging system for high throughput cell screening' and the 'live cell imaging microscope' as well as the ever increasing need for general data storage."

Valuable Resources. CMRI researchers Drs Roger Reddel, Phil Robinson, Antony Braithwaite, Megan Fabbro and Edna Hardeman were joint recipients of infrastructure grants from the Cancer Institute NSW worth \$1,722,104. These funds will support the NSW Cancer Proteomics Infrastructure Initiative, a Transmission Electron Microscope with Tomography and Flow Cytometry Facility. This state-of-the-art equipment, located at various sites in Sydney, will benefit CMRI cancer and muscle research projects in the future.

Investigator Travels. Noel Dowling Memorial Fellow Dr Samantha Ginn won the prestigious Young Investigator Award at the recent Australasian Gene Therapy Society conference. As part of her award Samantha will travel to the British Gene Therapy Society meeting in Edinburgh next year.

Heart Beats. Cardiologist Dr Eddy Kizana has described the use of a gene transfer vector, developed at CMRI, to deliver a gene into heart cells. Eddy, who was a PhD student in the Gene Therapy Research Unit and is now at the Johns Hopkins University, USA, has now shown that this vector can reduce electrical activity in the heart cells of rats. This approach may be useful for the future treatment of abnormal heart rhythms.

Members of the **Judith Hyam Memorial Trust** bade farewell to cancer researcher Dr Clare Fasching, CMRI's Judith Hyam Research Scholar for the last 6 years. Clare was overwhelmed when trust members presented her with a personally scrap-booked album and a beautifully decorated cake.



Diana Mahony with Dr Clare Fasching at her farewell

Jeans for Genes®

'Jeans on the Greens Golf Day'

Everyone had a wonderful time at Jeans on the Greens in May at Oatlands Golf course. The weather was perfect and someone even got a hole in one! Following the great day, a fundraising dinner was held and in total over \$12,000 was raised.

'Dare-Devil Denims – Jeans for Genes Art Auction'

This year the 'Jeans for Genes Art Auction' was kindly sponsored by Toyota Financial Services. Once again personally signed jeans from international celebrities were generously donated to CMRI and painted by Australian artists turning them into our unique trademark of fabulous Jeans for Genes artworks. The artworks were exhibited at The Arthouse Hotel launch and then auctioned at the Jeans for Genes Art Auction at the Four Seasons Hotel Sydney on July 12. A record amount of \$32,000 was paid for the well-known comedian HG Nelson's jeans, which were painted by Robyn Ross. John Glover from Pendragon not only bought them but also put in a bid of \$21,000 to secure Arnold Schwarzenegger's jeans painted by Garry Fleming. The night was filled with laughs and great music from the John Field band. The raffle prize, a once in a lifetime holiday to Vietnam, was kindly donated by Vietnam Airlines and The Leading Hotels of the World.

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Do it with Denim® Jeans for Genes Designs 2007

This year the 'Do it with Denim Jeans for Genes Design Awards' included two new categories, interior design and high school entries. The standard of the garments and pieces of furniture was extremely high and made the judges' decisions extremely difficult. The National winners of each category were: Fashion Design – Cyan Reign of Metropolitan South Institute of TAFE, Queensland; Interior Design – Mary Harrington of Lidcombe TAFE NSW and the School Award went to Alyssa Du-Shane from Alexandra Hills High School, Queensland.

Jamm for Genes®

'Jamm for Genes', now in its second year, was a fabulous success with over 100 venues and bands taking part. From Darwin in the Northern Territory to Bunbury in WA, Wodonga in VIC and Newcastle in NSW musicians across Australia got together to raise funds for the CMRI. Events ranged from a performance by Opera Australia of 'The Barber of Seville' at The Opera House to 'Pops for Tots' in Penrith and many major events in Sydney. On Thursday August 2 there was the 'Country Jamm' at the Canterbury Hurlstone Park RSL Club where James Blundell, Becy Cole, Adam Harvey, Stacey Morris and The McClymonts all got together, with many other performers, and played their hearts out. Then on Saturday August 4 at the Gaelic Club we had Glenn Shorrock and friends Brian Cadd, Ian Moss, Mark Gable, John Swan, Jade MacCrae, Jenny Morris and more jammed the night away. The night was a fantastic success to say the least!

Launch of the new Jeans for Genes Website

Check out our website – it is fresh and new www.jeans4genes.com.au

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



Kambala School students at Edgcliff Station, Sydney



Leeming High School volunteers in Perth



Elyse Chiert volunteer Genie at Bondi Junction Station, Sydney



A fabulous Jeans on the Greens Golf Day team



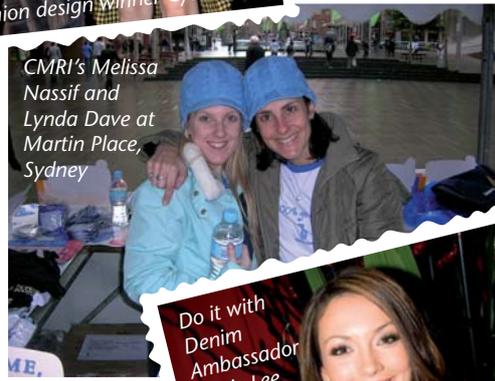
Fashion design winner Cyan Reign



CMRI scientists and friends at Darling Harbour



Jamm for Genes Genies at the Gaelic Club



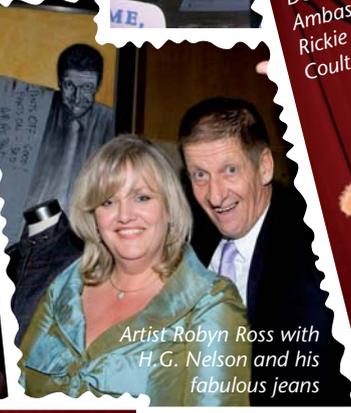
CMRI's Melissa Nassif and Lynda Dave at Martin Place, Sydney



Auswide Projects in Cooma, NSW



Jeans for Genes Ambassador Sabrina Houssani (former Miss World Australia)



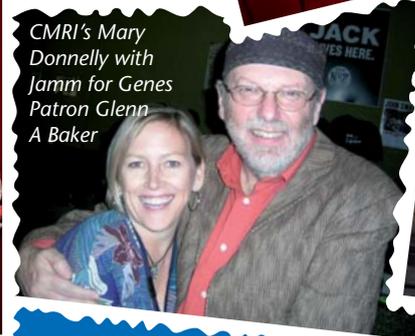
Artist Robyn Ross with H.G. Nelson and his fabulous jeans



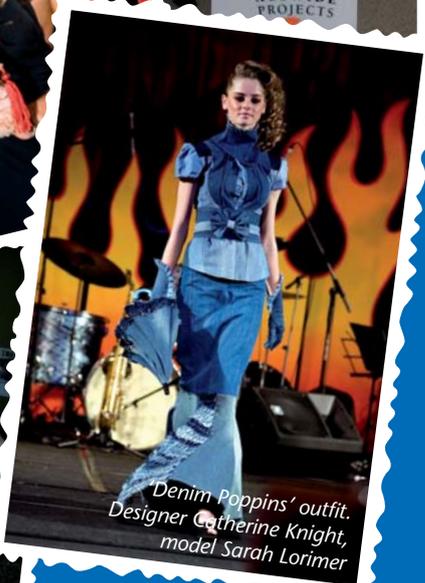
Do it with Denim Ambassador Rickie Lee Coulter



CMRI's art auction volunteers



CMRI's Mary Donnelly with Jamm for Genes Patron Glenn A Baker



Denim Poppins' outfit. Designer Catherine Knight, model Sarah Lorimer

Children born with cataracts



Dr Robyn Jamieson and PhD student Marija Mihelec who are working on cataracts in children

We usually think of cataracts as being a disease of the old but, surprisingly, congenital cataracts – cataracts present at birth – account for 10% of childhood blindness worldwide. Seen as cloudiness of the lens, up to 70 genes are believed to be involved in causing this condition and both human families and mice are being studied to identify these genetic causes.

Almost the entire sequence of human DNA is now known and it is consequently easier to identify the genes responsible for a wide range of conditions, including congenital cataracts. So Dr Robyn Jamieson, leader of CMRI's Eye Genetics Research Group* within the Embryology Unit, and her team are working hard to identify some of these genes.

Dr Jamieson and PhD student Marija Mihelec have recently discovered a fault in a previously unrecognised gene on chromosome 16 in a young child with congenital cataracts. The gene is normally switched on in eye cells at the edge of the lens.

In a separate family, Dr Jamieson also identified an error in another human gene called *MAF*. Mice with errors in three different parts of this gene have since been found to exhibit cataracts. By studying one of these, Robyn and co-workers in Manchester, UK, have now revealed how this particular error in the *Maf* gene causes blindness.

At present, children born with cataracts undergo surgery early in life to restore their vision. After surgery, Robyn and co-workers have discovered the affected children unfortunately have a 15% risk of developing glaucoma (increased pressure in the eye). "This is important information as glaucoma can cause blindness if it is not detected and treated early," says Robyn. "The Eye Genetics Research Group is also investigating glaucoma genes to improve treatment for this condition."

These results have been published in the journals *Human Mutation*, *Human Molecular Genetics* and the *British Journal of Ophthalmology* and were achieved with collaborators at Manchester Royal Eye Hospital, Manchester University; Western Sydney Genetics Program at The Children's Hospital Westmead and Save Sight Institute at the Sydney Eye Hospital.

*The Eye Genetics Research Group is a joint initiative between CMRI, the Western Sydney Genetics Program and the Save Sight Institute.

Driving CMRI Research Forwards

If you drove on the M4, M5 or Eastern Distributor on Tuesday 22 May, then your toll has gone towards raising \$117,000 for the CMRI. This generous donation has just been used to purchase a state-of-the-art microscope, with real-time imaging equipment, for observing the early stages of development.

The high resolution 3-D images that can be captured by this equipment will enhance the capability of CMRI embryologists to track the movement of cells and the formation of early organs as the mouse embryo develops. Such studies will provide a valuable insight into the causes of birth defects of the head, eyes, face and palate, and the impact of abnormal cells on brain function. "This builds on the almost complete 'fate map' of the mouse embryo that my team has elucidated over the last sixteen years, which is now recognised as an invaluable reference point for developmental biologists worldwide," says Professor Patrick Tam, Head of the Embryology Research Unit.

For the last three years, CMRI has been a charity of choice for the motorway operator's annual collection of toll money for charity. Funds from the last two events, \$309,500, went towards the cost of CMRI's mass spectrometer facility, which has been instrumental in discovering the composition of telomerase – an enzyme involved in 85% of cancers. This finding has brought the development of new anti-cancer drugs a step closer (winter 2007 newsletter).

Thank you to the Drive for Charity Funds team and all motorists who contributed to this major research investment.



Drive for Charity's Mr Eric Roozendaal (Minister for Roads and Minister for Commerce) and Mr Brendan Bourke (Chairman, Airport Motorway Limited, Interlink Roads Pty Limited and Statewide Roads Limited) presenting a cheque to CMRI's Stephen Ryall



Committee Power

Committees

Taree Committee teamed up this year with the Taree Craft Group and other craft enthusiasts for show-and-tell demonstrations, fabulous morning teas and a grand raffle.

Mothers and daughters who attended the **Hills Committee Mother's Day Luncheon** enjoyed a stylish event, featuring a fabulous cooking demonstration by celebrity chef Kylie Kwong and her mother Pauline. Over 570 diners were also entertained by MC John Mangos and singer Sabrina at the event which raised \$26,000.

Many thanks go to the **Gosford Committee and the East Gosford Lions and Lionesses** who recently purchased a biosafety cabinet for our biosonicator, an essential research tool. The new biosafety cabinet will protect CMRI researchers as they work.

At the **Racquet Club Committee** card day a full house of active bridge players enjoyed a relaxing and entertaining day with delicious lunch and tea.

Congratulations to the **Quirindi Committee** who celebrated their 40th birthday with a luncheon in July, attended by Acting Director Dr Roger Reddel and his wife, Clinical Associate Professor Helen Reddel. Quirindi Committee have raised almost half a million dollars for CMRI over 40 years – a truly amazing achievement.

Other Supporters

The **Rotary Club of Cessnock Wine Country** held another wonderful fundraising event for CMRI in the beautiful Hunter Valley.

At the annual **BMW Trivett Golf Day** glorious weather and the spectacular course at Riverside Oaks provided the perfect backdrop for the golf day. A very generous donation of \$8,800 was presented.

Many thanks go to the **New England Credit Union** who organised a spectacular black-tie **Winter Wonderland Charity Ball** in Armidale. The event was enjoyed by 190 guests including CMRI's Acting Director Dr Roger Reddel and his wife Helen.



Dates for your Diary

Wednesday 12 September

Joey Fimmano Concert "Italian Delight" at Rooty Hill RSL Club. Contact Diana Mahony 02 9630 5572.

Saturday 22 September, catch the excitement at the Hills Committee CMRI Charity Race Day at Rosehill Gardens. Fabulous luncheon, drinks and fashion prizes. Contact Sharon Finnigan 02 9687 3767.

Thursday 18 October Her Excellency Mrs Marlena Jeffery will be Strathfield Committee's special guest speaker at Parliament House. Contact Sue Goff 02 9744 7428.

Friday 9 to Sunday 11 November

visit Gerringong Quilt Show, with a fabulous display of quilts, stalls etc. Contact Dorothy Hambridge 02 4234 1346.

Friday 9 to Saturday 10 November

head down to Wagga Wagga Christmas Fair, with over 90 stalls of original Christmas gifts. Contact Rhonda Walmsley 02 6926 3555.

Wednesday 14 November Book now for the Canberra Committee's famous Garden Luncheon at the magnificent property "Red Brow" Murrumbateman, just past Poacher's Pantry. Numbers are limited so please book early. Contact Celia McKew 0419 445 041.

Clockwise from far left:

CMRI's Jennifer Philps with Robyn Lauder, Heather Bramble and Pat Eyb from Taree;

Jenny McFadyen, Drs Helen and Roger Reddel and Josh Faulkner at the New England Credit Union Ball (photo courtesy The Armidale Express);

Gosford Committee President Alison Elms with East Gosford Lions and Lionesses and the new safety cabinet;

Simon Macedone (General Manager BMW Parramatta) with CMRI's Jennifer Philps and James Jancu (Marketing and Events Manager);

Mrs Joan Moses (original committee member) and Mrs Jean McDonald (longstanding member), cutting the 40th birthday cake – with President Pam Lord;

Kylie Kwong with her mother Pauline.

