

under the microscope

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"Thank you Australia for... Getting in on the Act"



Seven year old Jacqueline Facaris and her sister Katelyn know only too well what it means for a family to live with a rare genetic disorder. Jacqueline has metatropic skeletal dysplasia, or as Jacqueline calls it "bad bones". The genetic cause behind her disabling and painful condition is unknown and there is no cure.

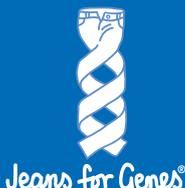
Jacqueline's mother Linda, a volunteer at CMRI, gave an inspirational presentation about the ups and downs of her family life at the Jeans for Genes Art Auction. She hoped to raise the profile of genetic disease and encourage people to get in on the act and support the cause.

Three generous bidders certainly did decide to support the cause on the night and bought Delta Goodrem's jeans painted by Garry Fleming for \$11,000. They donated the jeans straight to a delighted Jacqueline Facaris – one of Delta's youngest fans!

The Children's Medical Research Institute would like to thank everyone who wore their jeans in support of Jeans for Genes Day 2004. In its 11th year the campaign is still considered one of Australia's largest special event days on the calendar.

Jacqueline and Katelyn Facaris with jeans once owned by Delta Goodrem. The pants were auctioned as part of the Jeans for Genes Art Auction and later donated to Jacqueline. (Photo by Sandra Priestley, courtesy The Sunday Telegraph)

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Director's desk



The research community, which of course includes all CMRI supporters and donors, is always complaining that governments do not

support the Australian research effort to a level comparable to that

experienced in other first world countries. Governments do, however, respond to community pressure. With an upcoming Federal election on 9 October we must make our interest and concerns clear to the candidates from all parties. If governments get the impression that research is not a priority issue for society they will not respond.

The Coalition Government, now in caretaker mode, failed to release the long completed Grant Report into the effects of the increased funding to the National Health & Medical Research Council which is the major source of support for medical research in Australia. It is believed, unofficially, that the report was extremely positive and urged further expansion of funding in the future. Whether any announcement on this important matter will be made as a "sweetener" prior to the election is questionable. More disturbing perhaps is the lack of any clear research policy statement by the Labour opposition. Perhaps this is also being held back for political reasons.

Nevertheless, I would urge all of those who are supportive of medical research to lobby their local candidates and let them know you have a concern. While the principal research groups are exerting pressure in many ways, nothing is more effective than grass roots support. Scientists are perceived quite rightly to have a vested interest and your involvement is critical.

On a lighter note, the Institute is deeply grateful to all who worked for the success of our Jeans for Genes appeal. Although competition for funds is increasingly fierce it would appear that we have maintained our level of support in 2004.

Professor Peter Rowe

Dr Tracy Bryan receiving her Young Tall Poppy Award from Frank Sartor at the Australian Institute of Political Science



Flowers are in Bloom

Spring came early for CMRI as Dr Tracy Bryan was awarded a NSW Young Tall Poppy Award. Since the presentation from the Australian Institute of Political Science, Tracy has become a local media starlet, with articles featured in the Parramatta Sun, Hornsby Advocate and the Sydney Morning Herald's Lab Watch and Sydney Magazine.

The Tall Poppy Awards recognise the achievements of Australia's young researchers for their outstanding scholarship, international achievements and effective public communication.

Dr Bryan, Head of the Cell Biology Unit returned to CMRI in 2001, after working in the USA, to continue her study of the telomerase enzyme.

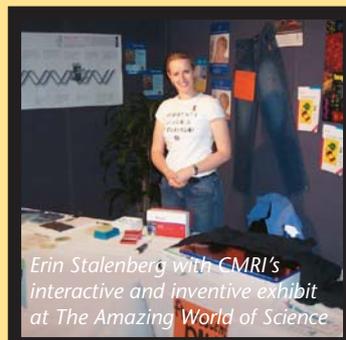
Telomerase is active in up to 90 percent of cancers. Tracy first studied this enzyme during her PhD under Dr Roger Reddel in the Cancer Research Unit at CMRI.

Tracy explains, "Cancer occurs when normal cells begin to grow out of control. Normal cells stop growing because each time they divide the ends of their chromosomes, known as telomeres, shorten. Eventually they get so short the cell gets a 'stop' signal. In cancer, telomerase adds DNA to the end of chromosomes, so these cells never get the stop signal."

Dr Bryan's research aims to fully understand how telomerase works so that new drugs can be designed to kill cancer cells by attacking the telomerase enzyme. "Current cancer treatments are effective but cause a lot of collateral damage, such as hair loss and nausea. Telomerase is specific to cancer cells, therefore a treatment based on this will hopefully leave normal cells alone."

The Amazing World of Science

Poisonous snakes, magnetic meteorites, smart robots and GENEius CMRI experiments. This was just some of the slick science on show during National Science Week's premier event The Amazing



Erin Stalenberg with CMRI's interactive and inventive exhibit at The Amazing World of Science

World of Science exhibition in Canberra from 18 to 22 August. The event brings science to the public in a fun and down-to-earth way, aiming to enthuse young and old about the wonders of science.

Erin Stalenberg from CMRI wowed thousands of visitors with fluorescent DNA, mouse skeletons, bacterial clones, brains down a microscope and Michael Jordan's jeans.

The event was hailed a huge success by local media and national visitors. The organisers, the Australian Science Festival, commended CMRI for the accessible and interactive science on show.

Double the effort for Doublecortin

A concerted team effort by two laboratories at CMRI has resulted in a big leap forward in understanding the function of a key protein involved in brain development.

The Developmental Neurobiology Unit and the Cell Signalling Unit pooled their considerable expertise and used CMRI's state-of-the-art mass spectrometry facility to solve a major puzzle of how the doublecortin protein helps nerve cells move into position to wire up the brain.

Their findings have been published in the prestigious *Biochemical Journal*. The journal commended them on the new and very thorough approach they took to achieve this exciting result.

Mutations in the doublecortin gene lead to a severe form of mental retardation known as lissencephaly. In this condition neurons are not neatly arranged in the characteristic layers of the cortex, the outer most part of the brain. The disorganised neurons cannot make the right connections to communicate with one another.

"This work shows the strength of CMRI's broad based research philosophy, bringing together a critical mass of expertise and equipment to get the job done thoroughly."
*Dr Peter Jeffrey,
Head of the Developmental Neurobiology Unit.*



Dr Mark Graham of the Cell Signalling Unit and Dr Patricia Ruma-Haynes of the Developmental Neurobiology Unit worked closely together on the brain protein doublecortin

Scientists in the USA recently identified that a protein called CDK5 helps doublecortin do its job. Mutations in the gene that makes the CDK5 protein also disrupt the layers of neurons – a clue that the two proteins may work together.

"We have confirmed these scientists findings and have taken the research much further. In fact the interaction of the two proteins is much more complex and interesting," said Dr Patricia Ruma-Haynes of the Developmental Neurobiology Unit.

CDK5 activates doublecortin by adding a chemical group called a phosphate. Key to understanding how doublecortin works is knowing where the phosphate is added. This will reveal why mutations in certain parts of the doublecortin gene cause disease.

"In addition to the site identified by the other scientists, we found two additional target sites for CDK5 on doublecortin that are potentially more important in the neuron" said Dr Ruma-Haynes.

Dr Mark Graham in the Cell Signalling Unit worked closely with Dr Ruma-Haynes to use the mass spectrometry facility – a state-of-the-art tool for analysing proteins – to conduct a thorough hunt for these sites.

The Cell Signalling Unit was already expert at finding the targets of CDK5, having published results on dynamin in a high profile paper in *Nature Cell Biology* last year (see August 2003 issue at www.cmri.com.au). "We knew that we could be missing some information with our previous methods, so we developed a more thorough approach to help the Developmental Neurobiology Unit," said Dr. Graham. "It's a very intensive approach, but we can be very confident that we haven't missed anything."

Weakness is Mai-Anh's strength

Congratulations to Mai-Anh Nguyen of the Muscle Development Unit on winning first prize – twice – for her research poster on the muscle weakness disorder, nemaline myopathy.

In early June, Mai-Anh presented her poster at the Australian Society for Medical Research NSW meeting held as part of Medical Research week. The week is held to raise the profile of medical research in the community and gives young scientists an opportunity

to present their work to colleagues. Mai-Anh then entered the same poster as part of the Westmead Association's Hospital Week and won first prize again!

Mai-Anh's poster described the group's findings on the mouse model for a severe form of nemaline myopathy, caused by mutations in the actin gene, which forms an essential part of muscle fibres.

"We have shown that the mice have the same microscopic features in their muscles as

seen in the human disease," said Mai-Anh, "this indicates that the mice will be a useful model system to study how the actin mutations cause the unique characteristics of severe nemaline myopathy."

Mai-Anh shared the first of the prizes jointly with her colleague Biljana Ilkovski from the Neurogenetics Research Unit at The Children's Hospital at Westmead. Biljana's poster described the changes seen in the muscles of humans with nemaline myopathy.



Mai-Anh Nguyen in the laboratory at CMRI

Jeans for Genes Thank you...

Continued from page 1

An estimated 3 million Australians took part this year and to date over \$27 million has been raised since Jeans for Genes began. It is always astonishing to note that the money is raised by simply wearing your jeans and giving a donation, or buying one of our three pins.

Art Auction

The Jeans for Genes music-themed Art Auction was a huge success, raising over \$260,000 on the night. This could not have happened without the support from major sponsors including The Leading Hotels of the World, Malaysian Airlines, Aussie Home Loans, Royal Brunei Airlines and Air Mauritius.

Mick Jagger's jeans painted by portrait artist Nafisa Naomi was the highest selling pair of jeans on the night, selling for \$25,000.

Chris Bath from Channel 7 generously gave her time again to be a wonderful master of ceremonies and special guest performers Kamahl and Cosima De Vito provided fabulous entertainment. Music historian Glenn A. Baker provided some music trivia and then ripped open a package with a surprise pair of jeans from his buddy, three time Oscar winner Tim Rice. John "Aussie" Symond purchased the jeans painted on by artist Robyn Ross for \$12,000.

Do it with Denim

For the "Do it with Denim" Fashion Design Competition tertiary students redesigned second hand jeans into a wearable garment with a music theme. Australia-wide 260 students took part in the event. State finalists' garments were exhibited on national television and at the Arthouse Hotel and Charlie Brown's signature store in Sydney. The winner, Cherileen Bull from Western Australia designed a stunning streetwear-style two-piece denim garment fit for any rock and roll celebrity.

Jamm for Genes

New this year were the Jamm for Genes concerts in Melbourne and Sydney proudly sponsored by Jeans West, the State Theatre, Sydney and the Esplanade Hotel, Melbourne. Over 700 people attended the concerts to see bands such as Machine Gun Fellatio, Thirsty Merc, Dave McCormack and the Polaroids, Taxiride, and Gus and Frank.

Committee Power

Other major Jeans for Genes events included those organised by the wonderful CMRI Committees. A huge brownie bake-up was organised by the Young Committee, raising an

astonishing \$10,000. The Canberra Committee held a sophisticated Denim, Diamonds and Pearls cocktail party at Old Government House. The Port Hacking Committee enjoyed a special Jeans for Genes Dinner and the Griffith Committee's Denim and Lace Ball was a sparkling success. Congratulations to all the Committees and their enormously supportive local communities.

Support Nationwide

Jeans for Genes would like to thank the following official retail outlets for their wonderful support this year - Myer, Jeans West, Just Jeans, Big W, Best and Less, Gloria Jean's Coffees, Lowes, Harvey Norman, The Warehouse, Terry White Chemists, Toys R Us, HCF, Bayswiss, Sizzler, General Pants, Domayne, Levi's, The Pharmacy Guild of Australia, Franklins, Spendless Shoes, Rebel Sport, Rex Regional Airlines, Austar, Polo Ralph Lauren, Banjo's and Westpac Bank. Over half a million dollars will come from retail sales alone.

Lowes Menswear have extended their wonderful support by also donating 50c from every 'Men from Lowes' 2005 calendar featuring new Rugby League stars. (Available in all Lowes stores).

Then there are our Genies at schools, colleges, businesses and government agencies who took charge, co-coordinating the fundraising amongst staff and/or students. Jeans for Genes would not exist if it weren't for their continuous loyalty.

No event is too big or too small and Jeans for Genes need not begin and end with the Day. In a wonderful example of the type of inventive support we receive, young Fraser Cockburn from the King's School Preparatory School will donate the proceeds of his Year 6 enterprise project to the cause. Fraser's 'business' is t-shirt production. He has made a prototype and is now taking orders. The school will be holding their Jeans for Genes Day in November.

Now don't forget to put it in your diary – Jeans for Genes 2005 – Friday August 5.

Generous sponsors of the Dinner Auction

The Leading Hotels of the World, Ltd.
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Malaysia Airlines
Going beyond expectations

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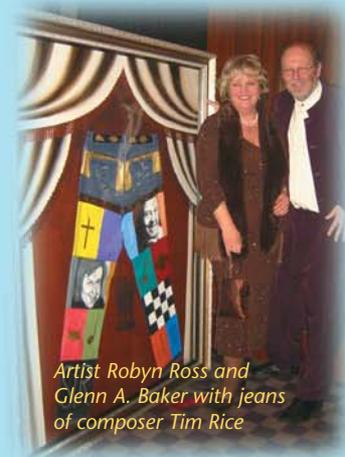
Air Mauritius



Cherileen Bull's winning denim design, worn by Mai-Anh Nguyen



Zeenia Kaul, daughter of CMRI Cancer Research collaborators, sold badges in four languages



Artist Robyn Ross and Glenn A. Baker with jeans of composer Tim Rice



Kyle, one of the many celebrities who donated their time to promote our merchandise

Staff at a Domayne's Fyshwick store getting in on the act



Winners of the Jeans for Genes colouring competition at the Whitsunday's Library with their prizes



Helpers at the Denim, Diamonds and Pearls cocktail party in Canberra (Photo courtesy Silas Brown)



Kamahl and the Brent Street Dancers entertaining guests at the Art Auction



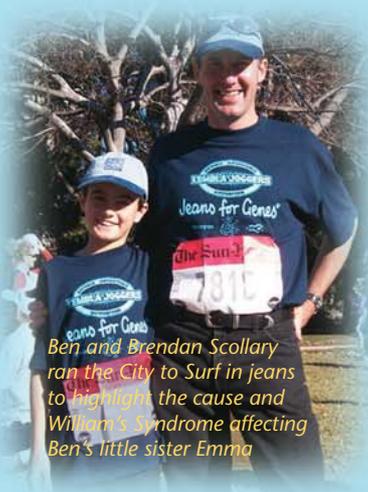
Art Auction MC Chris Bath with Majid Ghodusi, one of CMRI's scientists who volunteered on the night



Griffith Committee at the Denim and Lace Ball



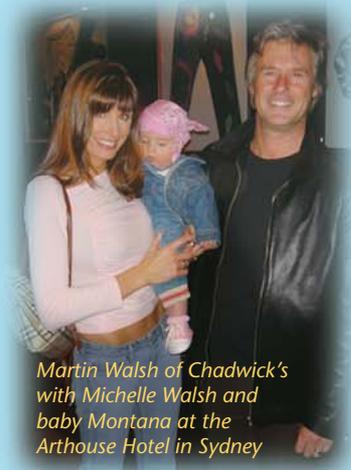
Krispy Kreme staff raised over \$4400 selling denim doughnuts



Ben and Brendan Scollary ran the City to Surf in jeans to highlight the cause and William's Syndrome affecting Ben's little sister Emma



This greyhound couldn't wait for Jeans for Genes Day



Martin Walsh of Chadwick's with Michelle Walsh and baby Montana at the Arthouse Hotel in Sydney



Melissa Doyle with Talia wearing the Bambini Cerrone bangle



Fraser Cockburn (centre) with friends Jack Rigg (left) and Chris Bruce (right)

"In over fifty percent of muscular dystrophies the genetic cause remains unknown. This discovery provides a new place to look for the genes." Dr Hardeman

New clue for muscular dystrophy

The discovery of an entirely new feature of muscle cells, never before described, has revealed a possible new cause of muscular dystrophy.

This amazing discovery was made by researchers in the Muscle Development Unit at CMRI in collaboration with Prof Peter Gunning's Oncology Research Unit at The Children's Hospital at Westmead. It was published in the very prestigious Journal of Cell Biology in August.

"We thought we pretty much knew all the structures to be found in muscle cells, but now we've found another one," says an excited Dr Edna Hardeman, Head of the Muscle Development Unit.

The structure is composed of actin and tropomyosin – two protein components that are common to the structures in muscle cells that allow them to contract, as well as the scaffoldings that give all cells their shape and ability to move. The two proteins come in different forms, giving the structures in muscles and non-muscle cells their different properties and functions.

The team had been busy trying to understand the role of a form of tropomyosin found in the non-muscle cells of the body. In the process they realised that it was in fact also found in muscle cells, but in an entirely new muscle structure.

"We are still not exactly sure what role this structure plays in muscle cells," says Dr Anthony Kee of the Muscle Development Unit, "but we know it's important because when we deliberately disrupt it in mice they get a form of muscular dystrophy."



Dr Edna Hardeman, Head of the Muscle Development Unit with Dr Anthony Kee

A microscope image showing the characteristic striped structures of muscle fibres. The new structure is stained in red.

Mice and humans are very different, but the team is confident they will find new answers to muscular dystrophy by hunting for the components of the structure in mice. "In the past where scientists have found genetic causes for dystrophy in mice, the genes have also been found to be involved in human disease. So it looks very promising," said Dr Kee.

The most common forms of muscular dystrophy are Duchenne's, which affects one in every 3200 boys and the milder Becker muscular dystrophy. In 1987, mutations in the dystrophin gene were discovered to be the cause of these two forms of dystrophy. Since then several other genes have been found, but in over fifty percent of muscular dystrophies the genetic cause remains unknown. This lack of knowledge leads to additional distress and difficulties for the many affected families.

The team is now working with Professor Kathryn North and her team in the Neurogenetics Research Unit at The Children's Hospital at Westmead. They will screen the many muscle biopsies taken from patients to look for possible mutations in components of the new structure.

Sounding a note of caution

CMRI scientists have made a discovery that should send a warning to scientists in diverse areas of medical research. "We have found that some cells used in experiments may not be as 'normal' as people think," says Jane Noble of the Cancer Research Unit.

The finding, published in the journal *Oncogene*, relates to the telomerase enzyme which is active in up to 90 percent of cancers allowing them to grow unchecked. The Cancer Research Unit and many other scientists have been studying telomerase for some years. They hope that it will ultimately be possible to kill cancer cells by blocking the action of telomerase.

As a reverse of this, scientists, including those at CMRI, are also using telomerase as a tool to prolong the life of cells used in research.

Scientists use cells grown in the laboratory to test their theories about biological mechanisms, test drugs, or even grow new tissues, such as skin grafts, for patients. Normal cells only grow for a short

time before they die, limiting their usefulness. Telomerase allows scientists to overcome this hurdle, effectively making the cells 'immortal'.

"Besides being immortal, these cells are considered by many to be essentially normal and therefore a useful experimental tool," says Jane. "We have shown that cells immortalised in this way can accumulate mutations in a number of genes involved in tumour growth. These cells are potentially several steps closer to being cancerous."

"Experiments on these cells can still provide valuable information," says Dr Roger Reddel, Head of the Cancer Research Unit, "but particular care will need to be taken if telomerase is used, for example, in tissue engineering applications to develop cell based treatments for patients."



Pictured from top:

Deborah Thomas, guest speaker at the Hills Committee's Mother's Day Luncheon, with her mother Mrs Lola Thomas and MC John Mangos;

Looking a million dollars, members of the Strathfield Committee celebrating their wonderful fundraising achievement;

Architect Harry Seidler with Cinzia Montresor of Opera Australia and pianist Simon Kenway at the Vacluse/Double Bay Committee Cocktail Soiree;

Brent Jones, Manager of Statewide Roads, with Professor Peter Rowe and one of CMRI's recent purchases, a mass spectrometer;

Students from Hennessey Catholic College with teacher David Johns and Erin Stalenberg after a dynamite talk on DNA.

Committee Power

SUPPORTERS

Porche day out

The Putty road gleamed with the 'porschist' cars around as they wove their way to Wandin Valley Estate for a wonderful lunch all thanks to Trivett Classic Parramatta and Mike Munro who organised the charity raffle for the CMRI.

BMW Classic golf day

Autohaus Classic BMW, Parramatta hosted their annual golf day at spectacular Riverside Oaks and again CMRI was delighted to be the beneficiaries of this most enjoyable event.

Charity Drive

CMRI was recently lucky enough to be one of few charities benefiting from the Drive for Charity day on 8 June. Thanks must go to Statewide Roads, operators of the M4, M5 and Eastern Distributor in Sydney, who donated all tolls collected on that day to various charities.

Earle Page College

Catwalks, cowboys, champagne and eye-catching fashion were all features at the Earle Page College Fashion Parade held in June. The Fashion Parade is just one of their fantastic annual events, with the main event being the Coast Run to Coffs Harbour. CMRI gladly accepted a cheque from last year's Coast Run for \$15,000 - a record amount!

COMMITTEES

Young Committee

Susan Hirst and the Young Committee played perfect hosts to Jennifer Philps and Erin Stalenberg of CMRI, who made a whirlwind trip to thank the Young community in NSW for their support of CMRI. The locals gained some insight into CMRI's genetic research with visits made to Young Public School, St Mary's Primary School and Hennessey Catholic College, the Rotary Club of Young and the Committee and friends at Zouch restaurant. Thanks also to local radio Star FM who enthusiastically promoted CMRI and Jeans for Genes Day during the visit.

Strathfield - Looking a Million Dollars

Congratulations to this wonderful Committee as they top a million dollars in fund-raising over the past 45 years.

Gerringong

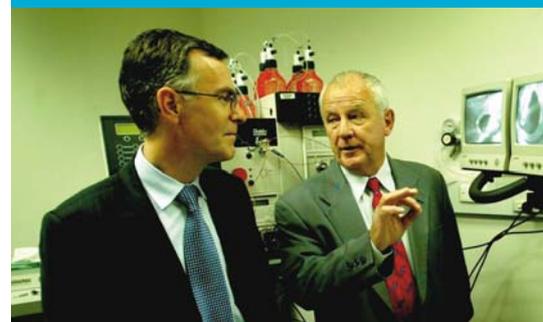
Many thanks to Gerringong Lions Club for their "Jumbo Charity Flight to Nowhere" when 300 lucky passengers enjoyed a spectacular flight over the South Coast courtesy of Qantas, Captain Mark Roche and his air crew. They kindly donated the \$11,000 raised to the Gerringong Committee of the CMRI.

Hills Committee

The annual Mother's Day Luncheon held at Sydney Convention centre was an outstanding success with Deborah Thomas editor-in-chief of The Australian Women's Weekly captivating the audience with the story of her life at "The Weekly". John Mangos also charmed the audience as MC.

Vacluse/Double Bay Committee

Mr Harry Seidler AC OBE spoke eloquently at the Cocktail Soiree at Designer Rugs showroom in Edgecliff beautifully organised by the Vacluse/Double Bay Committee. Many thanks to Cinzia Montresor of Opera Australia and pianist Simon Kenway for the entertainment.



How YOU can help us

Have you got a burning desire to help CMRI achieve its goals of a healthier future for all children? Have you got a flair for organisation and a streak of fun? If so then, you could be what CMRI is looking for... you could start a new committee. It doesn't matter where you are or what your do. Just gather your friends together, put your thinking caps on and start having fun for a good cause. For information call Jennifer on 02 96872800.

Dates for your Diary

Can Can Committee

Saturday Night Fever Disco Night, Avalon RSL, 6 November.
Tickets \$35. Contact Anna 02 9918 5331

Canberra Committee

Annual Luncheon in the fabulous grounds of Government House, Canberra, 18 November. Contact Carolyn 0418 284 788

Thumbelina Committee

Annual Trivia Night, Laurelbank, Laurel St, Willoughby. 16 October.
Contact Michelle 02 9412 1162

Strathfield Committee

Quiz Night with quizmaster The Hon. George Souris. Civic Centre, Devlin St, Ryde, 15 October. Contact 02 9980 9778
Thanksgiving Day Luncheon, at the American Club, 25 November.
Contact Nita 02 9980 9778

Northern Beaches Committee

Luncheon with guest speaker crime fiction author Gabrielle Lord, Royal Prince Alfred Yacht Club, Newport, 15 October, 11.30am.
Early bookings essential, contact Cheryl 0419 612 240

Quirindi Committee

"The Windy Woolshed Spring Ball" The Windy Woolshed is just outside Quirindi, NSW. 23 October. Contact Til 02 6747 1744

Wagga Wagga

Annual Wagga Wagga Fair at the showground, 5 and 6 November

Treasury of Crafts Christmas Craft Fair

Don Moore Community Centre, North Rocks, 3 December, 3pm – 8.30pm and 4 December, 9am – 3pm
Dural Memorial Hall, Dural, 18 December, 9am – 4pm

Goodwill Charity Card Shop

Open from 27 September to 17 December.
Level 1, WEA House, 72 Bathurst St, Sydney

CHRISTMAS CATALOGUE

The CMRI Christmas catalogue is out now, with beautiful Christmas cards, gift ideas and much more. To obtain a copy call **02 9687 2800** or visit **www.cmri.com.au**



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.

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Thanks for your help.