

# under the microscope

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## 11/10 Research at CMRI is 'lookin' good baby!

All around the country people were once again wearing jeans for this year's national *Jeans for Genes Day*. On train stations waves of blue legs walked through turnstiles and in conservative CBD offices, management and staff took to the day with fun and generosity.

And as if trying to find the answers to childhood cancers, muscle disease and more wasn't enough, scientists at CMRI also gave up their time to help in the fundraising effort. On Friday 2 August, CMRI scientists could be spotted at railway stations all over Sydney. Along with hordes of helpful school students, they were there to sell Jeans for Genes badges to an enthusiastic public.

"Community response continues to amaze and delight us. Once again we thank all the genies, particularly those who regularly help us by donating their time and money," said CMRI's Stephen Ryall, Jeans for Genes campaign manager for 2002.

"The funds from Jeans for Genes Day are invested in our capital fund and year after year the interest on this fund finances our research programs. Research is the only way medical science can find better treatments for genetic childhood diseases, and Australian businesses, schools and the community at large have shown that they support that."

*Continued page 4*

*Shown in the 'O' above is the growing limb 'bud' of a mouse embryo. The purple colouration shows the location of Twist gene activity. (See story page 3)*



*Letting the Genies out of the laboratory - ready to sell badges on Jeans for Genes Day are (left to right) Mark Corbett of the Muscle Development Unit and Kathy Baran, Lyndal McLure and Kylie Bower of the Cancer Unit.*



# Director's desk



The ground-breaking studies from the Embryology Unit

highlighted in this issue represent a major

step forward in developing a better understanding of the genetic basis to a wide range of congenital physical defects involving the face and limbs. These results are the outcome of years of intense research by a number of gifted scientists led by Dr Patrick Tam and reinforce the benefits of creating committed focussed research teams. The next question is, of course, why and how these specific genetic mutations occur.

The issue of human embryonic stem (ES) cells is under discussion by our elected Federal Parliamentary representatives with a view to creating legislation to control their use in a range of experimental activities. While accepting that the debate about the destruction of human embryos for research purposes is primarily an ethical one, it is relevant to note that, from a purely scientific point of view, arguments claiming the urgent need for ES cell research to 'cure' debilitating human disease are not compelling.

Undue expectations have been created in the community as to the imminence and scope of ES cell-based treatments and the major obstacles of immune rejection and cancer development have been generally ignored. The achievements of the therapeutic approaches using adult stem cells have been played down.

We have available the research animal models to effectively test whether ES cells have any role to play in the treatment of disease and this must be done prior to considering human subjects. Accordingly, from a scientific point of view there should be, in the interim, a moratorium on the destructive use of human embryos.

Professor Peter Rowe



Inspiring guest speaker, Mrs Susan Hirst, shared her story with the Auction guests.

## 'Generations' of generosity at the Jeans for Genes art auction

Different theme, same fantastic success! No artworks were done for the Jeans for Genes Art Auction this year, only paintings by 16 very talented and generous artists, created in their own style, on the theme 'Generations'.

After touring the exhibition to the Sheraton Mirage, Gold Coast and The Windsor Hotel, Melbourne in June, the 16 artworks were exhibited and auctioned in Sydney at the Art Gallery of New South Wales on 4 July.

Following a private tour of the Archibald, Wynne and Sulman exhibitions, the 280 guests who turned out for this gala event, viewed the Jeans for Genes artworks by artists such as Esther Erlich, David Boyd, Nafisa Naomi, Hugh Oliveiro, Judith White, Neil Taylor, as well as previous Archibald Winners, Adam Cullen and Euan Macleod.

Justin Miller, Chairman of Sotheby's Australia, auctioned the artworks, raising a stunning \$95,000. David Boyd again topped the bill, with his painting 'The Generations – The Eternal Return' fetching the highest price of \$22,000. (Limited Edition autographed prints of this painting are still available from the CMRI at \$100 each and can be viewed on our website).

In total the night raised over \$190,000, and we were superbly entertained by Channel 7's Chris Bath as MC and the stars of Opera Australia, Jacqui Moran and Seang Yoon Lee.

The guest speaker was Mrs. Susan Hirst of Young, NSW. Susan and her sons, Samuel and Broderick, suffer from a genetic condition called Epidermolysis Bullosa (EB or "Cotton Wool" babies). EB results in the layers of skin not adhering to each other properly, so the skin can blister severely from even the gentlest friction caused by everyday activities. Susan's son, Samuel, created his own artwork on a pair of baby Levis, which raised \$1,900 in the auction. Thank you, Susan, for sharing your inspiring story with us.

Many thanks to everyone involved in making the exhibitions and auction such a great success, including The Leading Hotels of the World, Taylor Made Travel, and Chloe Maxwell for her contribution at the Melbourne exhibition.



Channel 7, long-term supporters of Jeans for Genes, got into the generous spirit at the auction. Left to Right: MC Chris Bath, Denis Carnahan, Sally Flynn, Peter Lewis, Always Greener's Caitlin McDougall, All Saints' Erik Thomson, Geoff Hill (Managing Director Seven Sydney) and Anne-Marie Hill, Danny Raco and Ada Nicodemou from Home and Away.



Dr David Loebel studies the gene blots that allow him to identify new genes regulated by Twist.

Getting one set of experiments completed for publication is no mean feat. Yet the Embryology Unit has just published four papers in the space of two months! The team has untangled the twisted threads of a story about a gene called Twist that is proving to be a key player in the development of both head and limbs in an embryo.

## something to **Twist** and **Shout** about

In humans, mutations in *Twist* cause a rare disorder called Saethre-Chotzen Syndrome (SCS) which is associated with malformations of the face and skull (craniofacial) and extra or missing fingers and toes.

Although SCS is very rare, understanding the genetic pathways behind the syndrome is the key to understanding many similar disorders. "There are a large number of human syndromes in which we see both craniofacial and limb abnormalities together," says Dr David Loebel, a post-doctoral scientist in the laboratory. "We now have strong evidence, that *Twist* is a central coordinator for several pathways of interacting genes that choreograph head and limb development. Because the paths are interlinked a mutation in any one of these genes would lead to similar malformations."

The product of the *Twist* gene belongs to a group of proteins known as transcription factors that switch other genes on and off. The team has used several different approaches to discover which genes *Twist* is regulating.

Two outstanding PhD students, Meredith O'Rourke and Kenneth Soo, have studied the effects of mutating *Twist* in mice and confirmed that the gene is essential for normal development of the head and limbs. They showed that *Twist* has a major effect on two key molecules that mediate communication between cells. And they have also confirmed that *Twist* directly controls two genes, *Alx3* and *4*, previously suspected to have a role in the *Twist* line of command due to the similar abnormalities the genes cause when mutated.

Dr Loebel's role in the project has been to hunt for new genes that form links in the chains leading out from *Twist's* control hub. "We were extending the study beyond

preconceived hypotheses of genes suspected of operating in the same pathway, to discover entirely new genes."

Dr Loebel used a painstaking technique to sift through thousands of genes and find the ones whose activity was altered in the developing limbs of *Twist* mutant mice compared to normal mice. Dr Loebel identified 49 genes, but four of these turned out to be particularly interesting because they have never been described before. "All four show an overlapping pattern of activity with *Twist* in normal mice and are not switched on at all in the mutant mice. This is a clear indication that they are directly controlled by *Twist*," says Dr Loebel.

*"This is quite an effort of my colleagues!" says Dr Patrick Tam, Head of the Embryology Unit. "These four papers have filled a significant gap in our understanding of development and the causes of some birth defects."*

"We still don't know what these genes are. They have no similarity to any known genes so it is not possible to even guess at what their role is, but it's going to be exciting to find out!"

But how can one gene have such major effects on two such diverse parts of the body as the face and limbs? "There is an evolutionary theory that the segment of the body containing the jaw was duplicated to give rise first of all to the forelimb segment, and then later in evolution duplicated again to produce the hind limbs," says Dr Loebel, "also, both jaw and limbs grow out as extensions from the body, so it's not so surprising that they require similar genes to control that outward growth."



Dr Roger Reddel with Pat Farmer

## Running in for a visit

Ultra-marathon runner turned Federal Member for MacArthur, Pat Farmer, took time out of his busy schedule of parliamentary duties, charity runs and family commitments, to pay a recent visit to CMRI. Jany's Allan of the Allan Research Trust (ART, which raises money for CMRI's Cancer Unit) had met Pat at a recent function and she inspired him to come and see for himself what we are achieving.

Pat showed enormous interest in the facilities and research at CMRI and was keen to learn how fundraising could help us do more. Pat has tackled some of the most arduous long distance runs, including the 72hr slog across the Simpson desert. So he was particularly interested to learn about the mass spectrometer, a machine that can turn the marathon of medical research into something more like a 100m sprint! And this got Pat thinking about the challenge of finding another \$1 million to upgrade the mass spectrometer so that it can help us perform even greater feats of protein identification.

Whilst at CMRI Pat also took the opportunity to ask plenty of questions to update his science knowledge and so help with some of the complex issues they must tackle in parliament.

# CMRI research and Jeans for Genes, lookin' good ...

*Continued from page 1*

Since 1994, the Jeans for Genes campaign has raised around \$20 million (and that excludes this year - those funds are still rolling in)! During that short time those funds have enabled the CMRI to open 3 new laboratories - the Gene Therapy and Cell Signalling Units and most recently, the Cell Biology Unit. And, whilst research 'breakthroughs' don't just happen overnight, the Jeans for Genes campaign has helped our scientists achieve a significant number of new findings. For example, we have gained new insights into the way cells become cancerous; discovered a number of new genes thought to be involved in mental retardation, cancer and osteoporosis; we have uncovered new information on the muscle weakness disorder nemaline myopathy and gained new understanding of how gene activity 'pulses' rather than being a constant 'on' as previously thought. We have also been able to purchase a new mass spectrometry facility

that enables CMRI scientists (and others in the Westmead Research Hub) to analyse hundreds of proteins in a day. And, there are many more additions to the international store of medical knowledge too numerous to mention here.

So, to all our genies, schools, businesses, committees and the general community we say 'thank you' for helping us in working towards our vision of a healthier life for future generations of children.

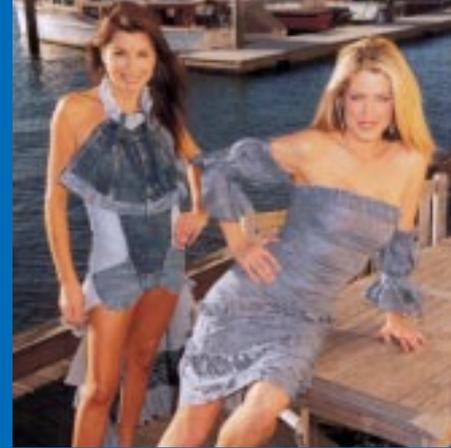
## **Denim wherever you look!**

In Melbourne, Fox FM's morning pair Tracy and Matt had an easy job auctioning *Sex in the City* star Sarah Jessica Parker's Jeans. The jeans painted by Melbourne artist Yvonne Sherring-Howard raised \$4000. And Carlton footy club players ditched their usual kit and took to the field with their children to help raise awareness of the big day!

Also getting behind the campaign this year were Tara Moss and Michelle Walsh who generously donated their time to model some stunning designer denims created especially for Jeans for Genes.

Down at Royal Randwick in Sydney, on 10 August, the Ball Committee of CMRI got together with Australian Jockey Club Young Members to put on a Jeans for Genes Race Day cocktail function. Here denim gave way to the finest frocks and hats, but as well as having a flutter on the horses, punters dug deep to bid on auction items such as Tara Moss' jeans painted by Hugh Oliveiro.

And Renee Zellweger's jeans, painted by Ester Erlich, were up for grabs to anyone who hired the Nurse Betty video or DVD through Movies 4U, Movieland or Universal Pictures. The competition raised \$15,000 for Jeans for Genes Day - fantastic!



*From top to bottom:*

*Model genes: Michelle Walsh (left) wears Gwendolynne and Tara Moss (right) wears Paablo Nevada (courtesy of Chadwick Management, Photo Brian McInerney – Strawberry).*

*Punter Amy Smith places her bets with bookmaker Ash Johnson Jr of Topodds.com.au at the Jeans for Genes Race Day.*

*Carlton FC players, left to right: Adrian Hickmont, Matthew Lappin, Captain Brett Ratten and Darren Hulme brought their kids along for a J4G photo shoot.*

## **Knit one, purl one ... creating a Jeans for Genes gem**

In pursuit of HSC excellence, Year 12 student, Katrina Zacharias, of St Euphemia College in Bankstown, NSW, has knitted a beautiful Jeans for Genes quilt for the major design project for her Design and Technology HSC.

"I was really inspired by the Jeans for Genes campaign," says Katrina, "it is my favourite charity. Every year the whole school puts on their jeans and makes a donation. It creates a great atmosphere and it's a great cause."

Katrina's innovative design has the core of CMRI's work woven into its very fabric.

"The knitted wool represents the coiling of the DNA strands into the chromosomes that contain our genetic material," says Katrina, "drop a stitch and the message will be corrupted, leading to disease and disability." Over this she laid appliqué motifs, using denim "to represent the day." The images of babies and childhood toys, mirror the aims of CMRI to find the knowledge that will help provide a happier, healthier future for all children.

A clever idea, and the result is a beautifully made, colourful quilt. No dropped stitches here!



*St Euphemia student Katrina Zacharias with her Jeans for Genes quilt.*

# Konnichiwa Dr Polly-san!

Dr Patsie Polly of the Muscle Development Unit has returned from a very productive working trip to Japan with exciting new data and techniques that will greatly benefit research in the Unit at CMRI.

Dr Polly won a Short Term Invitation Fellowship grant from the Japan Society for the Promotion of Science to work in Dr Sunil Kaul's laboratory at the National Institute of Advanced Industrial Science and Technology (AIST) in Tsukuba, Japan. The Australian Academy of Science also contributed travel costs for the international collaboration. Dr Kaul and his wife Dr Renu Wadhwa are already valued collaborators of CMRI scientists after they spent a sabbatical year in the Cancer Research Unit eight years ago, with another three-month visit in 2000. Now Dr Polly has been able to benefit from their expertise and technologies in Japan.

"I was able to generate a substantial body of work, and this was really driven by my daily discussions with Dr Kaul and Dr Wadhwa," says Dr Polly, "I was very excited by the prospect of freely exchanging ideas that led to successful experiments."

In particular, Dr Kaul, an expert in single cell microinjection, trained her in the technique of injecting tiny amounts of protein directly into

a cell. This will now allow Dr Polly to study the impact of certain proteins on the activity of genes in muscle cells. "I am working on a protein called MusTRD that we think is involved in specifying muscle fibre type," says Dr Polly.

Muscle fibres come in two main types, fast and slow twitch, that allow us to do different activities such as sprinting or maintaining our posture, respectively. Without the right balance of muscle fibre types our capabilities are compromised. "The techniques I learnt in Japan will be crucial in defining the exact role of MusTRD and help us find the other proteins that it works with. Ultimately this will help us to understand certain muscle diseases and give us the clues we need to correct the problems," says Dr Polly.

"Despite the huge amount I achieved professionally I was also able to get out and see a few of the sites! The Japanese people were so hospitable. The visit has had a profound impact on me."



Dr Patsie Polly (centre) with Drs Kaul and Wadhwa (far right) and their team



## 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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*Clockwise from top:*

*Thumbelina Vice-president Lesley Pitts with Neil Sheffield of Emirates, 'Italian Affair' raffle winner Lionel Desanges and Ivan Poupouras of CIT.*

*Earle Page College coast run convener, Stephen Gadd presents the cheque to CMRI's Bernadette Hanna, watched by run founder Brent Gregory and Master of the College, David Ward.*

*Polo player Andrew Ashton braves the rain with keen local kids at the Canobolas Committee's polo luncheon.*

# Committee Power

## **They're off to Italy!**

Congratulations to 'Italian Affair' raffle winners Lionel Desanges and Tracy Galbraith. The Thumbelina Committee gives special thanks to Emirates Airline, The Leading Hotels of the World, CIT, Anna Cuisina, Barilla, Bertolli, Cantarella Bros, Ferrari, Ferrero, Lavazza, Paul's Ltd, Sanpellegrino, Tibaldi and Un Momento Restaurant.

## **Denim dazzlers!**

Guests at Griffith's Dazzling Denim Ball had the opportunity to bid for two artworks; Jimmy Barnes and Peter Brock's jeans both painted by artist Simon Moseley, and were entertained into the small hours by The Mersey Beats. Thanks to Griffith Ex-servicemen's Club, and to Griffith High School students for their excellent waitressing.

## **Canobolas**

Despite soggy conditions the annual polo luncheon was great fun with a beautifully decorated marquee, warm braziers and delicious lunch. Grateful thanks to James and Susan Ashton for the use of 'Millamolong'.

## **Allambie**

As well as some serious golf at the annual Golf Day at Mona Vale Golf Club, there were fun events, including a competition to hit a hole-in-one into a boat on a waterhole! Congratulations to Margaret Naylor for her skilled shot.

## **Earle Page College**

The College has run up a great charitable record, raising over \$100,000 for the CMRI in the last few years with their annual Coast Run. CMRI scientist Bernadette Hanna attended the College's dinner to receive the cheque for last year's run.

## **Wamberal**

A warm welcome was given to the new president Margaret Hart at the annual luncheon at Avoca Beach Bowling Club. An enormous debt of gratitude goes to outgoing president Gwen Murphy.

## **Blackheath Golf Club**

Freezing conditions did not deter the golfers at the Ladies Open Charity Day. The theme 'Pearl Day' saw them dressed up in their finest pearls and even a tiara was on show!

## **Jazz in the Mountains**

Many thanks to Beecroft Rotary who again excelled themselves with this wonderful event. Together with generous sponsorship from Autohaus Classic BMW of Parramatta, a donation of \$20,000 was raised.

Autohaus Classic BMW has also made a huge contribution to CMRI via their Golf Day, held at Riverside Oaks in May.

## **Blacktown**

Many prizes and fun gifts made the annual Jeans for Genes Quiz Night a great success. Thank you to Quiz Master Rob Neil of 2WS.

## **Kell's Creek Vineyard**

Kell's Creek Vineyard near Mittagong is supporting young local artists by providing space to hang their works at the cellar door. First up is 16-year-old, award-winning photographer Rebecca Hallowell, who will donate a percentage of her sales to CMRI.



## **Dates for your Diary**

Allambie Luncheon, 13 September

Quirindi Race Day, 12 October

Canberra Luncheon, 12 November

Hills Committee - Floral Art show at 'Glenhope', West Pennant Hills, November 23 and 24.

This heritage farmhouse will be gloriously decorated with Christmas flower arrangements by the NSW Floral Art Club.

## **And for all your Christmas needs:**

Wagga Wagga Fair, 8 November

Gerringong Quilt Show, 8 November

Maroota Fair, 10 November

Strathfield Luncheon, 28 November

Treasury of Craft, Carlingford, 6/7/8 December

Goodwill Charity Card Shop, open 8 October – 18 December, Sydney Mechanics' School of Arts Building, 4th Floor, 280 Pitt Street.

*For details of all events call Jennifer Philps on (02) 96872800*