

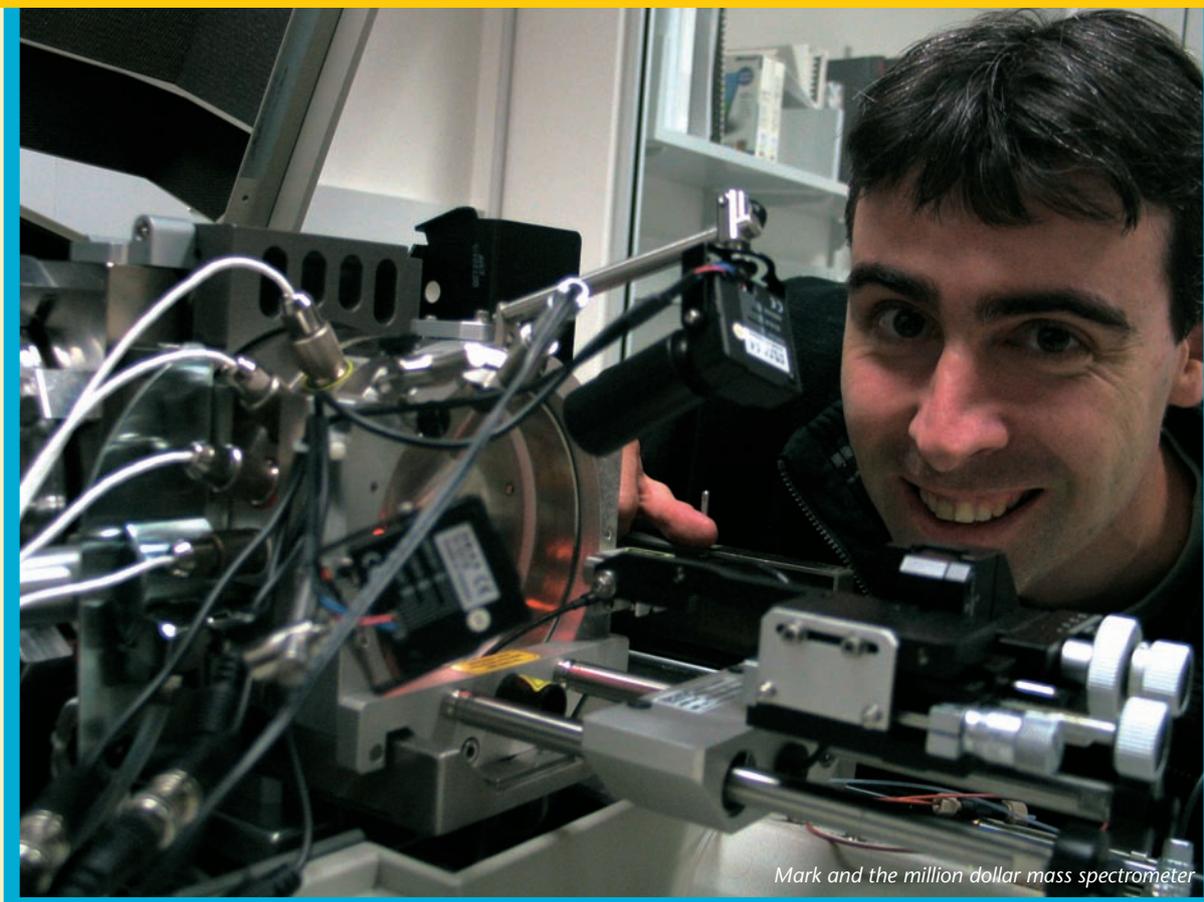
under the microscope

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Mark and the million dollar mass spectrometer

The Best ATM!

ATM money machines seem really important in our everyday lives, but a different kind of ATM found within our cells is even more important. The ATM protein kinase recognises DNA breaks that can occur within the cell and alerts the cell's DNA repair machinery. This is crucial because cells containing unrepairable DNA breaks need to be eliminated from the body, as they can lead to cancer.

The importance of ATM kinase is highlighted in individuals who have a genetic disorder called ataxia-telangiectasia. These patients inherit a mistake in the gene for ATM kinase and produce a defective protein. One of the problems suffered by these individuals is a susceptibility to developing tumours because their ATM kinase cannot repair damaged DNA.

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**CHILDREN'S
MEDICAL
RESEARCH
INSTITUTE**

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Director's desk



For the first time in umpteen years this column is not coming to you from Professor Peter Rowe. As you will know, he has retired from the helm of the CMRI, and we wish him all the very best.

What he has left behind is a vibrant research institute that works on complex questions of fundamental importance in human biology and development, for the simple reason that we need the answers in order to transform future medical practice.

Despite the apparent explosion of knowledge, the biomedical sciences are still in their infancy and whole new areas that we didn't even know existed are opening up. The research for which Andrew Fire and Craig Mello were awarded the Nobel Prize in Physiology or Medicine earlier this month is a pertinent example.

They discovered a process called RNA interference, which is used by cells to control the output of genetic information. It helps to defend against viral infections, and to keep our genomes stable. Only eight years ago we were unaware that this mechanism existed. It is now the basis of revolutionary new tools to study the function of genes, and it may well lead to novel therapies in the future.

Due to the generosity of our many supporters, CMRI is in the fortunate position of being able to obtain up-to-date research technologies. Many of these instruments use the extraordinary developments in computing power that have affected so many areas of our lives, and they allow us to look at cells and the molecules of life in completely new ways.

Peter Rowe has left us a research facility that is not only well equipped but also staffed by top-quality researchers. This is a wonderful foundation, and it is essential that we continue to build on it.

With your support, that's what we intend to do.



Roger Reddel
Acting Director



When bad p53 is good!

As part of an international study, Roger Reddel (Head of our Cancer Research Unit) and Antony Braithwaite (Head of our new Cell Transformation Unit) have used their joint expertise to help identify positive markers for glioblastoma patient survival.

A glioblastoma is a type of brain tumour, which can occur in children and is the most common form of primary tumour in adults.

Surprisingly, the scientists have discovered that patients with mutations in the tumour suppressor gene *TP53* have a better life expectancy than patients whose tumours have a normal copy of the gene. This is an important finding as mutations in the *TP53* gene have previously been found to predict a poor outcome for cancer patients.

It appears that *TP53* mutations in this type of cancer can activate the Alternative Lengthening of Telomeres (ALT) mechanism, one of the mechanisms by which cancer cells can achieve unrestricted growth.

"This is the first time that a defective *TP53* gene has been clearly linked to ALT activation during tumour growth and development," said Dr Roger Reddel, "and it can no longer be used as an indicator of poor outcome in this group of patients. The finding that *TP53* is involved with ALT and glioblastomas is a follow-up of our finding in 2003 that the presence of ALT in glioblastoma is an indicator of a better prognosis."

The Best ATM!

Continued from page 1

CMRI scientist Dr Mark Graham in collaboration with Martin Lavin's team at the Queensland Institute of Medical Research has analysed ATM kinase using CMRI's million dollar mass spectrometer.

The scientists found three positions within ATM kinase that were modified by a phosphate group when normal cells were damaged. Interestingly, when ataxia-telangiectasia patient cells were damaged, phosphate groups were not added, but adding normal ATM kinase back into the patient cells enabled them to signal again in the same way as a normal healthy cell.

The results tell us a lot more about how cells respond to damage to protect against forming a cancer. Understanding such signalling events in our cells will help in the search for new anti-cancer drug targets.

This work was just published in *The EMBO Journal* and was supported by the ARC.



Satomi and Yasuka
in the Embryology Unit

A Very Important Transport Gene

Egg and sperm cells have only half the number of chromosomes as a regular cell. For these germ cells to develop, therefore, an immature germ cell has to undergo a process called meiosis, during which the genetic material contained in a cell will be halved.

Yasuka Yamaguchi and Satomi Tanaka, of the Embryology Unit have been asking the question, when and how do sperm and egg cells, known as germ cells, first form within the body? And they have recently reported that a gene called Importin 13 is involved in this process. As the name of the gene suggests it acts as a shuttle, for the importation of factors (cargoes) from the cytoplasm into the nucleus of the cell.

Germ cells express the Importin 13 gene, which encodes two versions of the Importin protein a long form and a short form. For her PhD research project, Yasuka found that the long form is made in germ cells when the chromosomes separate - during the early phase of meiosis.

This protein is used to transport another protein called UBC9 from the cytoplasm into the nucleus. By reducing the amount of Importin 13 in the egg cells, less UBC9 was transported into the nucleus and meiosis was slowed down.

The short form of Importin 13 is identical to the long form, except for the absence of a part of the protein that allows the cargo to be released into the nucleus. The short form may compete with the long form to take up the free cargo, but cannot release the cargo into the nucleus, resulting in lower protein function.

Dr Patrick Tam, Head of the Embryology Unit says, "This novel transport mechanism may have relevance in systems other than the testis and ovary. Defective Importin 13 may lead to mental retardation and other genetic diseases may also be caused by the inefficient transport of protein."

Discovering Science at CMRI

From Year 10 science students to great-grandmothers, we have been promoting the benefits of science and medical research by showcasing CMRI's state-of-the-art facilities.

Nearly 300 members of the general public have attended our Discovery Days throughout the year, for an entertaining introduction to genes, a talk by one of our eminent researchers and a tour of our laboratories.



Marija Mihelec with Discovery Day visitors

If you or your group would like to see medical research up-close and personal, and are interested in attending a Discovery Day, please contact Jennifer Philips on 1800 436 437. Discovery Days run once a month from 10am-2.30pm and include a delicious morning tea and lunch. There is a nominal charge of \$15 pp.

STOP PRESS – Grant Successes

CMRI scientists Dr Phil Robinson, Dr Edna Hardeman, Dr Roger Reddel and Dr Ian Alexander have just been awarded over **\$2 million** of highly competitive NHMRC funding.

A further **\$1.3 million** in joint grants involving CMRI scientists has also been awarded to Dr Patrick Tam, Dr Edna Hardeman and Dr Ian Alexander and their respective collaborators. This is a great result as the NHMRC only funds 20-25% of the applications it receives, and it highlights the strength of CMRI research.

Dr Alexander is head of a joint research unit between CMRI and The Children's Hospital at Westmead (CHW).

Jeans for Genes® Update

To date Jeans for Genes Day® has raised over \$3.3 million. This is \$300,000 more than the same time last year. Congratulations to everyone involved. It seemed like every man and his dog wore their jeans, including some lovely pooches who wore their coats proudly on the day. We are already planning next year's big day – **FRIDAY AUGUST 3 2007**. So make sure it is highlighted in your diary.



If you haven't as yet sent in your money please do so before the end of the year. If you have any queries please call 1800 GENIES or 1800 436 437 (our new number).

Upcoming Events

The search is on for the FUJIFILM Australian Child Photographer of the Year! A sum of \$10 from every entry will go to Jeans for Genes.



The Aussie Kids Photo Festival has been specifically created to promote and celebrate creativity in young children. It is a unique event that will recognise, encourage and reward the early development of kid's photographic talents.

Children aged between **3 and 7 years old** are invited to enter their photos in the following categories:

- Self-Portrait
- Friends & Family
- Tallest Building
- Landscape
- Animals
- My Favourite Photo

To enter go to www.aussiekidsphotofestival.com

The Great Debate

The Great Debate is on again! 'Music is Better than Sport – or is it?' The event will once again be held at The Sydney Conservatorium of Music in May 2007 and will be hosted by the Royal Automobile Club of Australia. All proceeds will go to Jeans for Genes. In May 2006, celebrities such as: Jonathan Biggins, Jane Rutter, Simon Tedeschi and Greg Mathews had the audience rolling down the aisles with laughter. Next year's event will be even bigger and better! For further information please contact Lynne Wilkinson on 02 8273 2318.



Volunteers Needed for Charity Christmas Gift Wrapping!

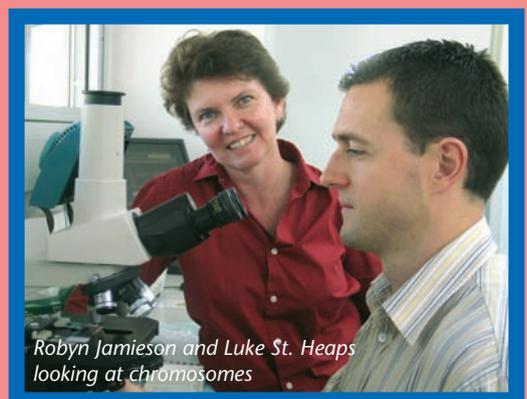
MYER have chosen Jeans for Genes as a charity partner and we need volunteers to help us gift wrap in December, before Christmas, to raise lots of money! It's easy. MYER kindly provide all the boxes and ribbon! We will be at Bondi Junction, Sydney City Store and Parramatta. For more details, contact Kelly Morgan on 02 9687 2800 or kmorgan@cmri.com.au

FISHing for blindness genes

Recent work on patients with anophthalmia, a condition where babies are born without eyes, is helping us to understand more about the genes that can cause this disabling eye disorder. Some patients are born with a chromosome translocation, where part of one chromosome has swapped places with part of another chromosome. In a few cases, CMRI and Children's Hospital at Westmead (CHW) scientists have been able to work out which genes are contributing to the blindness.

Using genetic techniques, including a method called FISH, scientists from our Eye Genetics research team and the Cytogenetics group at CHW, have been able to identify the point at which some chromosomes have broken. They have then identified six genes that are missing in some 'translocation' cases. From this work they have been able to deduce that the genes *OTX2* and probably *BMP4* are important for eye development.

"Chromosome deletions enable us to identify genes that might be affected in other cases of absent or small eyes, and in related eye disorders such as glaucoma," says Dr Robyn Jamieson.



Robyn Jamieson and Luke St. Heaps looking at chromosomes

Committee Power

COMMITTEES

Vaucluse/Double Bay Committee had a joint charity golf day for CMRI and young cricketers. Thank you to our eight talented teams!

Gosford Committee and Terrigal-Wamberal Lions Club purchased a brand new, high-tech PCR machine for our new Cell Transformation Unit. The 'Little Red Corbett' machine will be used by all the scientists at CMRI.

Strathfield Committee's Annual Quiz Night was a highly successful event. Quizmaster Stephen Ryall was outstanding and we are grateful for all the generously donated prizes.

OTHER SUPPORTERS OF CMRI AND JEANS FOR GENES

East Gosford Lionesses held a very successful Debutante's Ball at Gosford Central Leagues Club.

Muirfield Ladies Charity Golf Day was held at the beautiful Muirfield Golf Course. As usual the **Becroft Committee** craft and cake stall was a huge success.

Arden Anglican School students supported CMRI and their Mums organised a wonderful 'Denim and Diamonds' dinner. We would like to thank all for being so creative and supportive.

Blacktown RSL raised money for CMRI with its Jamm for Genes™ country music event. Many thanks for your generous support.

In late July, four intrepid cyclists from corporate sponsor **Thomas & Coffey** hit the roads around Kooralbyn, Queensland for a 12 hour 170km charity bike ride to raise money for CMRI.

Cultural exchange visitors from **Vladivostok** were keen to lend CMRI staff a hand with our Jeans for Genes Day mail.

St George School students visited the CMRI to present a cheque. It was fabulous to meet six wonderful teenagers and staff members.

Dates for your Diary

Friday 10 – Saturday 11 November. **Strathfield Committee** will be selling CMRI Christmas cards at Rhodes Shopping Centre.

Wednesday 15 November. **Canberra Committee Government House Luncheon** with a famously sumptuous lunch, stalls and a glorious historic setting. Contact Diana Ryan 0414 451 960.

Northern Beaches Committee will be selling charity cards at the following venues:
Monday 6 – Friday 17 November:
Forestway Shopping Centre.
Thursday 23 – Saturday 25 November:
St Ives Shopping Centre.
Monday 27 November – Friday 1 December:
Spotlight, Dee Why.

December 1 and 2. **Treasury of Craft Christmas Fair**, Don Moore Community Hall, North Rocks, with beautifully hand-crafted gifts. Contact Jennifer Philips 1800 436 437.

Sunday 17 December. **Tamworth Committee's Carols in the Park** with country singing and food. Contact Verity Bligh 02 6760 9242.

Saturday 6 January 2007. The **Allan Research Trust Race Day** at Sydney Turf Club, Rosehill Gardens. A major fundraising event for CMRI! Contact Janys Allan 0407 987 473 to be a sponsor with naming rights, signage and to sash the winning horse etc.

Don't forget to order your unique 'Beach and Bush Calendar Girls Calendar 2007' and CMRI Christmas Catalogue. Contact 1800 436 437.



Top to bottom:
Enthusiastic players at the charity golf day;
Gosford Committee with Professor Rowe and members of the Cell Transformation Unit;
CMRI's Jane Fleming accepting a cheque from Arden's Primary School Officers Nelson Noll and Emilie Duvé;
Russian volunteers at CMRI;
Dr Roger Reddel accepting a cheque from James Slack (cyclist) and Janie Gilmour, President of the Ku-ring-gai Committee.