

under the microscope

2 Cancer pothole filled

3 Brain breakthrough

4 Jeans for Genes

6 Olympics of Genetics



You're never too young to start getting into the Jeans for Genes spirit: Newborns at Sydney's RPAH Women's and Babies Clinic; Riccardo Ferraro, Tina Tesoriero and Calum Westbrook. Photograph by Melanie Fabbro, courtesy of Inner Western Courier.

You made our day! . . . Thank you

The Australian public have given Jeans for Genes Day a very special 10th birthday. To reach this 10 year milestone has been a wonderful achievement by the Children's Medical Research Institute and all Australians who participate in the day. To think, babies who were born on the first Friday of August 1994 (the first Jeans for Genes Day) are now 10 years of age and one in 20 of

those children will have a genetic disorder. It's a staggering figure. That is why CMRI began this campaign. It is one day where we ask all Australians to don their jeans, make a donation, have fun and remember it is for the health of tomorrow's children.

It will be some time before the final outcome is known for this year's

Jeans for Genes Day, but with records being broken on several fronts, our aim to raise \$4 million looks very much on target. This could not be possible without the passion and generosity of our Genies, Committees, retail outlets, artists and loyal supporters who helped us make our day so special this year.

Continued page 4



Director's desk



This issue highlights important experimental results from three of our research units recently published in major international journals. Roger Reddel's group has described one of the possible roles for a protein known as POT in regulating the activities of telomerase, an enzyme which is primarily responsible for the "immortality" of cancer cells. The protein is a possible target for effective cancer treatment.

The Cell Signalling Unit has published a major finding in relation to our understanding the mechanisms controlling chemical communication between nerve cells. This has significant implications for approaches to the treatment of disorders as diverse as epilepsy and schizophrenia.

Scientists in the Muscle Development Unit have expanded their knowledge of the function of a protein known as MusTRD, which they identified some years ago, and is critical for muscle development.

All of these studies represent important contributions to their respective fields and arise from focussed long-term research projects.

The staff of the Institute lost the services of our long-term Administrative Officer, David Sallows, after eight years of dedicated, committed management of our financial affairs. We wish him well in his retirement.

Once again, I wish to acknowledge the tremendous support from the community for our tenth annual Jeans for Genes® appeal which, even at this stage, would appear to be one of our most successful.

Professor Peter Rowe



Kathy Baran (left) and Dr Lorel Colgin (right) were key members of the team working on POT1

POT-hole **filled** in the road to cancer treatment

CMRI's Cancer Research Group has filled in yet another pothole on the long road towards finding an effective treatment for cancer. They have discovered how a protein called POT1 helps cancer cells to keep on growing and therefore how it could be blocked to help treat cancer.

POT1 (which stands for Protection of Telomeres) was discovered in yeast two years ago by a US research team headed by Nobel Laureate, Professor Tom Cech. The US team showed that POT1 helps to protect telomeres, the very tips of chromosomes, from degradation. The shortening or degradation of telomeres in normal cells is a key molecular barrier that limits cell proliferation. Most cancer cells avoid this barrier by activating a telomere lengthening mechanism.

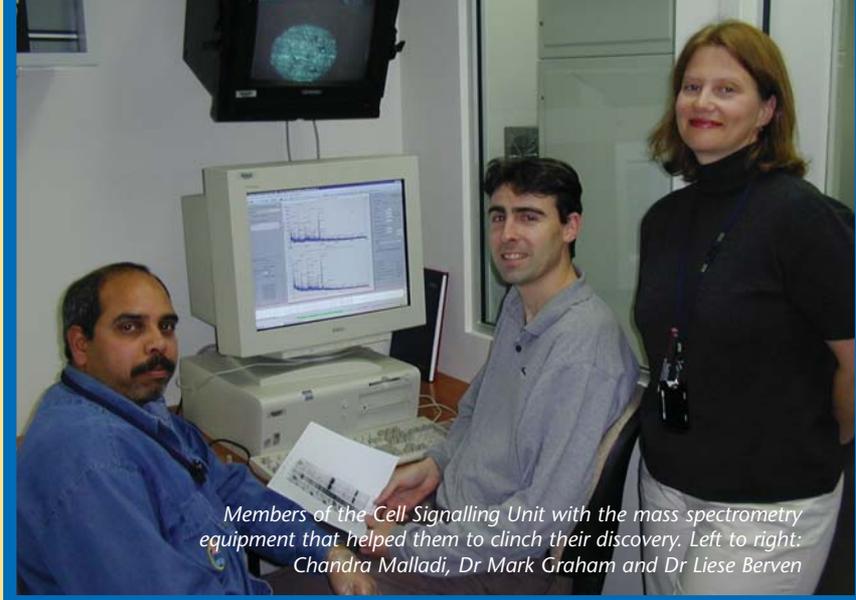
Dr Roger Reddel's team collaborated with Professor Cech to analyse the function of the POT1 protein in human cells and the exciting outcome of this work was published in the prestigious journal, Current Biology, in May.

"We found that cancer cells use POT1 to aid a key cancer cell enzyme, telomerase, in keeping the chromosome tip lengthened and therefore allowing cancer cells to multiply," said Dr Lorel Colgin, a key player in the team at CMRI along with research assistant Katherine Baran. "POT1 regulates telomerase, and may even act as the 'landing pad' for telomerase on the telomere end."

"This discovery has positive implications for future cancer patients. About 90% of cancers use telomerase to lengthen their telomeres and keep growing," she said. "There is a lot of excitement about the development of drugs that inhibit telomerase as a new form of cancer treatment. Our results suggest that telomere maintenance in cancer cells could also be disrupted by molecules that interfere with the interaction between telomerase and POT1."

Scientists in the CMRI's Cancer Unit have been able to pursue their work as a result of the fundraising achievements of Jeans for Genes Day and support from The Cancer Council NSW.

"The previous work was done in the test tube," says Dr Robinson, "but with our collaborator, Dr Mike Cousin, in the UK we conducted the experiment in living neurons, simultaneously on two continents and got the same result! CDK5 is the biologically relevant enzyme."



Members of the Cell Signalling Unit with the mass spectrometry equipment that helped them to clinch their discovery. Left to right: Chandra Malladi, Dr Mark Graham and Dr Liese Berven

Inner workings of the **brain** revealed

After the human genome has been fully deciphered, the human brain represents the last great unknown facing biological science. These were the thoughts expressed by several Nobel Laureates at the International Congress of Genetics held in Melbourne in July. (See story, page 6)

But Scientists in the Cell Signalling Unit at CMRI have already made a significant step towards unlocking the mysteries of the brain. The team, lead by Dr Phil Robinson, has just revealed in a paper in the leading journal Nature Cell Biology, that an enzyme called CDK5 plays a fundamental role in brain function.

CDK5 has previously been shown to be absolutely necessary for normal brain development and it is also involved in neurodegenerative diseases such as Alzheimer's. Now Dr Robinson's team have shown that CDK5 is vital, throughout life, for normal, everyday, communication between neurons.

The finding will ultimately have an impact on how we might potentially control nerve communication to treat diseases such as, epilepsy, schizophrenia, and memory and learning disorders.

Using four independent research methods the team has provided the evidence to neatly link CDK5 into the chain of events surrounding the release and recycling of neurotransmitters. Neurotransmitters are the chemicals that are released from one neuron at the synapse (the point of contact between two neurons) to trigger an electrical signal in the next neuron. They are packaged into tiny balloons called synaptic vesicles. Once the vesicles are emptied at the synapse they must be retrieved from the nerve ending, refilled and returned ready for the next round of signalling.

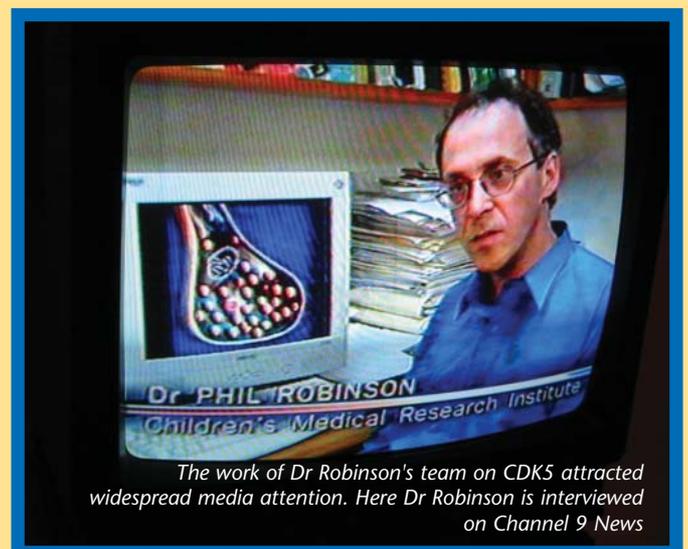
For the last 10 years Dr Robinson has been studying a protein called dynamin that behaves like a tiny molecular spring to effectively flick the empty synaptic vesicles back inside the nerve ending. This new work shows that CDK5 resets the dynamin spring ready for the next round of signalling. "Without CDK5, vesicles would not be refilled and neuronal signalling would grind to a halt," said Dr Robinson.

"In fact this knowledge suggests that if we could block CDK5, for example, we could potentially stop the uncontrolled trains of nerve signals that cause epileptic seizures. This is a long way off, but this discovery is the first step."

Importantly, CDK5 is only found in the brain, so altering its activity to treat brain disorders should not lead to side effects in other parts of the body.

In 1993, Dr Robinson had published work in Nature suggesting that an enzyme called PKC did the job of resetting dynamin, but now using state of the art technology such as the new mass spectrometry facility at CMRI, and specific drugs that block CDK5 but not PKC, Dr Robinson's team have proved him wrong.

"The previous work was done in the test tube," says Dr Robinson, "but with our collaborator, Dr Mike Cousin, in the UK we conducted the experiment in living neurons, simultaneously on two continents and got the same result! CDK5 is the biologically relevant enzyme."



The work of Dr Robinson's team on CDK5 attracted widespread media attention. Here Dr Robinson is interviewed on Channel 9 News

Pictured in the 'O' on the front cover is an electron microscope image of a nerve ending showing the tiny synaptic vesicles that contain neurotransmitters.

Happy 10th Birthday You made our day!

Continued from page 1

At the Jeans for Genes Art Auction held on 24 July 2003, Australian super legend Ian Thorpe broke another record - this time in the "Jean Pool," raising a whopping \$26,000 with his jeans painted by leading Australian portrait artist Paul Newton. The successful bidders were long-time supporters, Burwood Press. John Symond of Aussie Home Loans, was also a strong bidder buying three pairs of jeans, including, for a mere \$18,000, Hugh Oliveiro's intricate work on a pair of signed jeans from celebrity couple, Baz Luhrmann and Catherine Martin.

Ray Hadley did a superb job as the auctioneer and Chris Bath from Channel 7 was beautiful as always as our Master of Ceremonies. Special thanks must also go to Coby Godschalk and Fabian Ferretti who spoke and read a poem on the night about their beautiful daughter Gabriella who suffers from a rare chromosomal disorder. Overall it was a record-breaking night, raising approximately \$220,000 net – the most successful Art Auction in the history of Jeans for Genes.

Another magnificent, record-breaking result was at the railway stations in Sydney and Melbourne. In total over \$124,000 was raised. This would not have been possible without the school children and volunteers who were waiting from 6.30am to welcome the commuters arriving for work as they came through the turnstiles. The response from the general public was wonderful, with thousands of workers wearing jeans and buying badges.

Other exciting fundraising events included the Jeans Look Competition, which took place in Melbourne, Sydney and Brisbane. Over 500 children and teenagers participated. Winners walked away with an introduction to a modelling agency, a photographic portfolio from Starshots worth \$600 and a basketful of gifts.

Another event which took place around the country included the Redesigned Jeans competition where young designers from TAFE colleges designed outfits made out of jeans and denim. The outfits were paraded by dancers and each of the winners won a week's work experience at Studibakers, one of Australia's leading evening wear fashion houses.

There were many events throughout Australia which took place on the day and throughout July including Reggie's jeans from Big Brother being auctioned in Tasmania, the Superstars Unzipped Exhibition in Sydney and Melbourne, BBQ's at Warehouse stores, a major trivia night at the Olympic Hotel in Preston, Melbourne, an auction and fun run in full length jeans at Kembla Joggers in Wollongong, and an auction of a pair of jeans signed by the Newcastle Knights in Newcastle, to name just a few. This does not even include all of the wonderful events the CMRI committees have organised.

For the first time ever the Wiggles took off their trademark black pants and wore their jeans and the NSW State Ambulance Service also wore their jeans instead of their uniform for only the third time in 107 years!

What a year, what results, what a great success – THANK YOU! We look forward to doing it again bigger and better next year. Pop it in your diary now - Friday August 6, 2004.



Fletcher Humphreys, Chris Bath, Scott Major, stars from Channel 7 and friend at the Dinner Auction



John Symond and artist Hugh Oliveiro with Baz and Catherine's jeans



NSW State Ambulance staff in jeans with Channel 10's Tim Bailey



Jeans Look finalists in Melbourne



Swimming legend Susie Maroney, who donated her jeans for auction, with mum Pauline



Celebratory Cosmic baby cake made by genies in Tasmania



Jeans on the Harbour Bridge (Photograph Brian McInerney)



Redesigned Jeans finalists



Fabian Ferretti and Coby Godschalk at the dinner auction



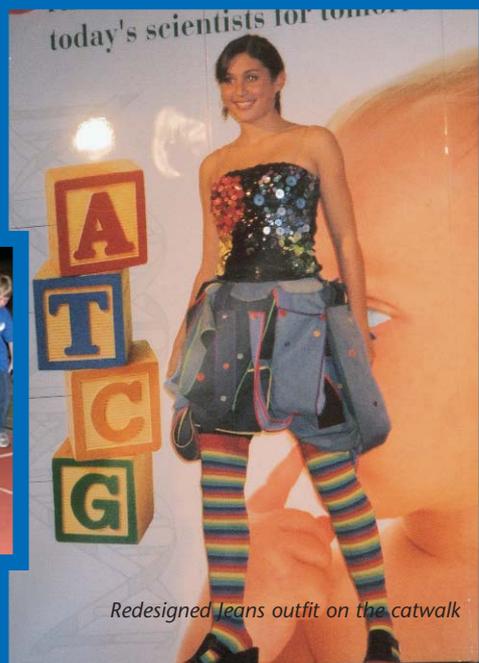
The Wiggles in their jeans



Jeans Look finalist on the catwalk



Jeans fun-runners at Kembla Joggers in Wollongong



Redesigned jeans outfit on the catwalk



Dinner Auction raffle bear



PhD student Enoch Tay and Dr Patsie Polly continue to decipher the results of their experiments to learn more about MusTRD

Fast or slow - MusTRD provides the answer

Scientists in the Muscle Development Unit have shown that a protein they discovered four years ago, called MusTRD, plays a key role in muscle development. The finding may help explain some of the symptoms of a rare genetic disorder called Williams syndrome and will contribute towards finding possible treatments for many muscle diseases.

The work has been published in two major papers in the prestigious *Journal of Biological Chemistry* and the *Biochemical Journal*.

It has long been known that muscle fibres come in two basic types: fast twitch for strength and speed and slow twitch for endurance. The correct proportion of each fibre type in each muscle is essential for proper function. Fibre type switching, changing from fast to slow and vice versa, can also happen in response to demands placed on muscles through training or in muscle disease. But until now it was unclear how muscle fibres become assigned to fast or slow.

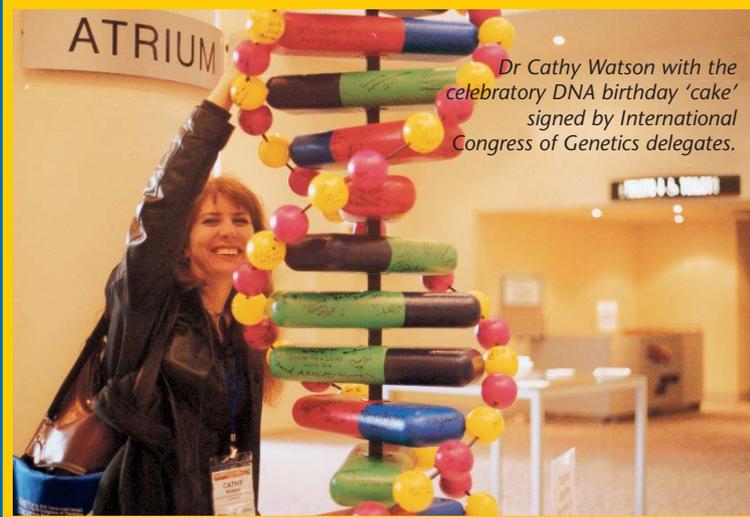
"MusTRD is one of the first proteins found that can switch muscle genes on or off, potentially telling the cell which type of muscle fibre to become," says Dr Patsie Polly, "this work places MusTRD as a very interesting player in fibre type switching."

The other exciting part of their work is the discovery that the MusTRD gene in mice, and probably in humans too, can produce not just one, but eleven, subtly different proteins. This is not unusual, but eleven is a relatively high number. "It makes analysing the function of this gene particularly complex," says PhD student Enoch Tay.

"What we've found so far is that each version of the protein is found in different amounts in different muscles," says Dr Hardeman, Head of the Muscle Development Unit. "It may help explain why some muscle disorders affect different muscle groups." For example, different forms of muscular dystrophy can affect facial muscles, limb girdles (pelvis and shoulders) or limbs.

In patients with Williams syndrome a small piece of chromosome 7, containing several genes, has been deleted. MusTRD is one of the missing genes. The most common symptoms are a heart defect and mild mental disability, but a poorly studied aspect of the syndrome is musculoskeletal changes. "With this new knowledge about MusTRD it might be possible in the future to address some of the other disabilities suffered by William's patients," said Dr Hardeman.

CMRI team at the "Olympics of Genetics"



Dr Cathy Watson with the celebratory DNA birthday 'cake' signed by International Congress of Genetics delegates.

The cream of the world's genetic research community converged on Melbourne in July for the International Congress of Genetics and a team of scientists were there to represent the CMRI.

The congress is held only once every five years and provides an unequalled opportunity for a truly international exchange of ideas and contacts.

With the theme 'Genomes: the linkage to life' the 2003 Congress celebrated the 50 years of phenomenal progress that followed the discovery of the structure of DNA by James Watson and Francis Crick in 1953 and culminated just recently with the completion of the sequencing of the human genetic code.

CMRI scientists were represented in many areas of the Congress. Dr Anthony Kee from the Muscle Development Unit presented a talk and his colleagues Mai-Anh Nguyen and Enoch Tay gave poster presentations of their work on muscle genes.

Dr Patrick Tam gave an overview of the Embryology Unit's work on the genes that control mouse embryo development. His colleagues, Drs David Loebel, Cathy Watson and Andrea De Young and PhD student Greg Pelka all generated interest from other delegates with their posters on developmental genes.

Dr Roger Reddel, Head of the Cancer Research Unit, took part in a symposium on telomeres and Dr Ian Alexander, Head of the joint CMRI-Children's Hospital at Westmead Gene Therapy Research Unit, brought together a group of excellent international speakers for a symposium on human gene therapy.

As well as mulling over the hard data, the delegates also made time to reflect on the social impact brought by progress in genetic science and the responsible use of gene technologies in the future.

Committee Power

Welcome – THREE new committees

Can Can Committee

Cabaret singer Anna Weaving found the CMRI cause so inspiring that she decided to start a new Committee in the Avalon area of Sydney. Her entertainment background gave rise to the Committee's motto of 'can can do do'! The new Committee is already showing what it can do with a Christmas in August lunch and a Salsa night.

Lakkariba Committee

Lakkariba, meaning place of the Banksia, is an apt name for the new committee based in the beautiful Wentworth Falls area in NSW's Blue Mountains. The enthusiastic new members gathered at the home of President Stephaney Packham for their inaugural meeting in June.

Young Committee

After giving an inspiring speech about the impact of the genetic disorder, epidermolysis bullosa, on her family at the Jeans for Genes Art Auction in 2002, Susan Hirst from Young in NSW, was determined to raise awareness and funds and the Young Committee was launched. Their first goal was to raise \$5500 for a much-needed refrigerated microfuge, but their first efforts have almost doubled that amount. Well done.

Cessnock Wine Country Rotary Club

Jennifer Philps of CMRI went along to a special party held to thank the Club's many community donors for their 40 years of giving to CMRI.

Hills Committee

Imagine TV personality, John Mangos' delight at being the only man in a room of 400 ladies at the annual Mother's Day Luncheon. His informal interview with impressive and successful mother and daughter team, Lillian and Jackie Frank, ensured a captivated audience.

Port Hacking Committee

The Irish band kept a full capacity crowd dancing amongst the scarecrows and hay bales at the Jeans for Genes Barn Dance. Thank you Port Hacking for raising a wonderful \$13,500.

Rotary Club of Strathfield

Many thanks to the Club for the cheque for \$6000 presented to CMRI by past president Stephen Taylor following the inaugural Olympic Park Bike Run.

Have a grapevine planted in your name

Kells Creek Vineyard in the southern highlands of NSW, owned by the Priebee family, will plant a grapevine for you in their Opi's vineyard, for \$250. \$100 of this is a tax deductible donation to CMRI. The vineyard is named after the family's much loved Opi (grandpa) who passed away from cancer last year. For more information phone Eric Priebee on 02 4878 5096 or visit www.cmri.com.au.

Thumbelina Committee

The Parisian atmosphere of the Pavilion on the Park and hard work and generosity of the Thumbelina Committee ensured the "Taste of France" evening was a wonderful success. Congratulations to the Grand Raffle winner Maureen Botha of St Ives who will enjoy a trip to Paris and the French Riviera courtesy of The Leading Hotels of the World and Travel World.

Pictured from top:

Four members of the new Can Can Committee, Alfia Vaisinni, Sue Gracie, Nada Waterhouse and Anna Weaving. Fifth member Anne Gelebert was overseas;

New members of the Lakkariba Committee at their inaugural meeting. Left to right: June Neville, Helen Boulden, Elizabeth Finlay, Marie Glass (sitting in front), Jan Gill, Stephaney Packham, Jan McCubbin, Olwen Henson and Robynne Aitkins;

The new Young Committee on a recent visit to CMRI's laboratories. Left to right: Jonathon Duff, Susan Hirst (holding Georgia Richens), Pip Crichton, Mary Lou Bomsembiante, Jo Hamblin, Sally Walker and Susie Duff;

Blackheath Ladies Golf Club President, Trish Thomson hands a generous cheque to Jennifer Philps of CMRI following their Ladies Charity Golf Day.



Committee Power - Dates for your Diary

Strathfield Committee

Annual Trivia Night with Quizmaster the Hon. George Souris MP.
Civic Hall, Devlin St, Ryde, 7.30pm, Friday 12 September

Gerringong Committee

Luncheon with guest speaker Barbara Holborow, Gerringong
Town Hall, 12pm, 19 September. And don't forget the Gerringong
Quilt Show, 7 - 9 November

Can Can Committee

Salsa Night at the Royal Prince Alfred Yacht Club, Newport,
with Salsa lessons and 3 course meal, 25 October

Port Hacking Committee

Life's a boat at the annual Putt Putt Regatta and picnic at Deeban
Spit near Audley, 26 October

Tamworth Committee

Carols in the Park with the South Bound Band and radio
personality Graeme Nuttal, 7pm, Sunday 14 December

Canberra Committee

Luncheon at 'Michalego Station' near Michalego (54 km south of
Canberra and 340 km south of Sydney). Well worth the trip.
12 November

'Blues' Weekend, Coleraine

Held in conjunction with the Coleraine Cup, the best Blues bands
will be at the National Hotel in Coleraine, Victoria. All proceeds to
CMRI. 27/28 September. Contact National Hotel on 03 5575 2064
for details.

Northern Beaches Committee

Luncheon at the Royal Prince Alfred Yacht Club, Newport, NSW,
with guest speaker Pat McDermott, Friday 17 October. And pick up
your Christmas cards from the Committee's stalls at Forestway
Shopping Centre and Spotlight, Dee Why from October

Judith Hyam Trust Fund for Cancer Research

Gala Charity Evening with music, comedy and dancing and special
guest host Channel 10 newsreader Ron Wilson. Hornsby RSL Club,
Saturday 25 October 8.30pm

Jazz in the Mountains

Jazz/Swing/Blues/Funk at 'Bisley' Mount Irvine Road,
Mount Wilson, 10.30am, Sunday 12 October.

Charity Card Shop - Sydney

Charity Christmas cards, including CMRI, on sale from 29
September to 17 December in the offices of the Workers'
Educational Association, 5th Floor, 72 Bathurst St, Sydney

For details of all events call Jennifer Philps on (02) 9687 2800

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:

\$100 \$75 \$50 \$25

Other \$

Please find enclosed my cheque

Please charge my credit card:

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
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 Information on how to make a bequest
 Please update your records for my contact details

All donations are tax deductible



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Thanks for your help.