

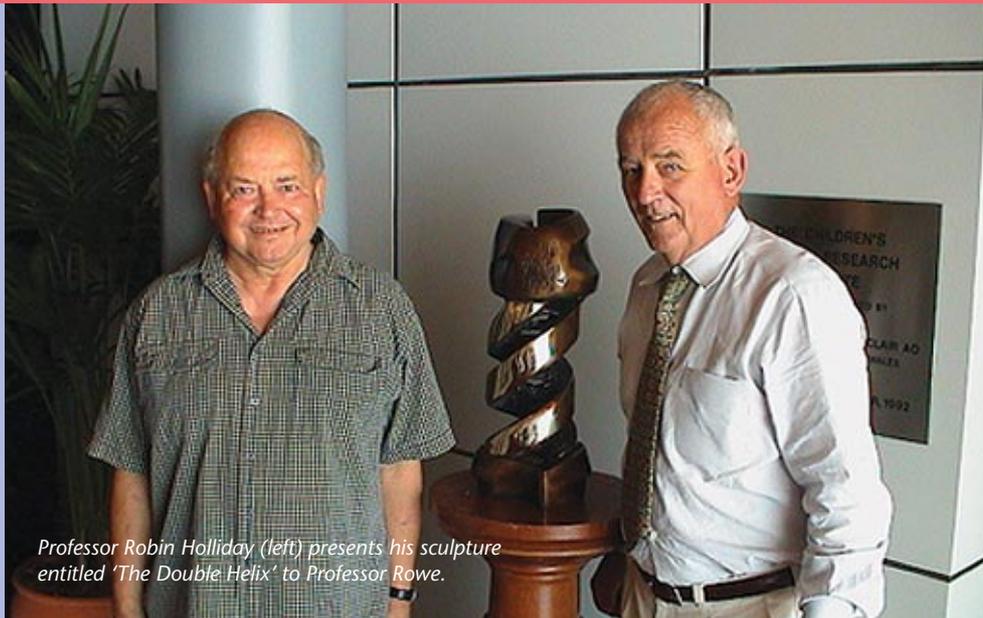
under the microscope

2 DNA Discovery

3 NHMRC grant successes

4 Jeans for Genes

6 Committee Power



Professor Robin Holliday (left) presents his sculpture entitled 'The Double Helix' to Professor Rowe.

2003 - a special year for the Double Helix

This year CMRI will celebrate the 10th birthday of Jeans for Genes® Day, but 2003 is also a very special anniversary for DNA! Fifty years ago two young scientists called Watson and Crick, working in the UK with their colleagues, unravelled the chemical structure of DNA and showed how this amazing molecule, shaped like a double helix, could hold the instructions for life itself.

The Jeans for Genes® logo, developed during our 1998 campaign, cleverly links the double helix DNA structure proposed by Watson and Crick to the jeans we wear. The denim double helix signifies the ongoing efforts of scientists at CMRI, with generous support from the Australian community, to build on the breakthroughs in medical science that began to flow following Watson and Crick's Nobel Prize-winning discovery.

In this special year CMRI has received a beautiful gift of a sculpture of DNA, with its associated proteins, by Professor Robin Holliday. Robin Holliday has been a major player in the field of DNA research, outlining in 1964, the mechanisms whereby chromosomes exchange genetic information.



50 years of DNA Discovery

A perspective from the Director's Desk...

It is now 50 years since the publication in Nature of the classic paper by James Watson and Francis Crick describing the basic structure of DNA. As is evident from a reading of Watson's version of the events surrounding their discovery in his 1967 best-selling book *The Double Helix*, only a relatively small community of scientists appreciated the immediate significance of their work. This is reflected in what today is perhaps the classical understatement of all time in the field of biological sciences in their paper, which begins, "We wish to suggest a structure for the salt of deoxyribonucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest. It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

I worked in major basic research institutions in the USA through the 60's and certainly many of the prominent scientists were rather dismissive of their achievement viewing them as opportunists who relied heavily on the primary work of Oswald Avery, Erwin Chargaff, Linus Pauling and most importantly the key contribution of Rosalind Franklin in putting their model together. Curiously, little mention is made today of the role of Maurice Wilkins, Franklin's superior and Head of the Crystallographic Unit at King's College in London, who was awarded the Nobel Prize together with Watson & Crick in 1962.

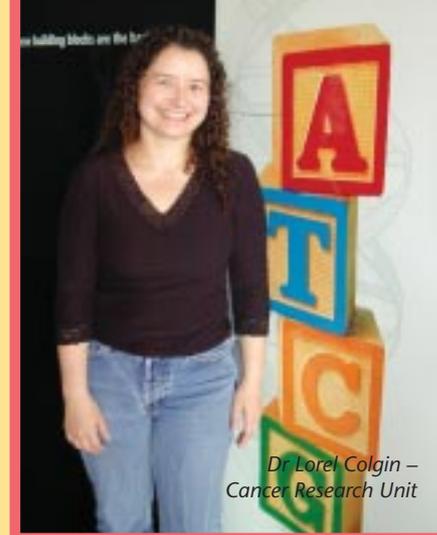
The attitude of many scientists to the discovery was interesting in terms of the direction of their own research "O.K. We have a structure, but how does it work?" This goal has dominated the last fifty years in biological research and although we have come a long way the answers are still quite unclear. Interestingly, attention has reverted to an intense focus on protein structure and function, the research area dismissed, if the Watson of 1951 is to be believed, as relatively uninteresting and unimportant. And so the cycle goes on.

Nothing, however, can detract from the fact that fifty years ago two unique, ambitious, focussed and gifted individuals were able to first describe the structure of a molecule that primarily determines what we are.

Professor Peter Rowe - Lorimer Dods Professor and Director.

The path to discovery

- 1886 – Gregor Mendel describes the laws of inheritance and proposes that discrete "factors" (or genes), are responsible for inherited traits.
- 1915 – Thomas Morgan confirms that genes are carried on chromosomes.
- 1941 – Beadle and Tatum confirm that genes direct the manufacture of proteins.
- 1944 – Oswald Avery discovers that genes are contained in the chemical deoxyribonucleic acid (DNA).
- 1950 – Erwin Chargaff discovers that the amount of each base, the chemical "letters" A, T, G and C, the building blocks of DNA, vary between species, but the amount of A always equals T, and G equals C.
- 1952 – Rosalind Franklin uses X-ray crystallography to resolve some features of the structure of DNA. Her unpublished work is shown to James Watson.
- 1953 – James Watson and Francis Crick, put the pieces of the puzzle together to produce a double helix model for the structure of DNA.
The model had two strands of DNA running counter to one another with paired bases, A to T and G to C, forming the rungs of a twisted ladder. The pairing of the bases suggested a mechanism by which the information contained in the strands could be copied to pass the information from cell to cell and from generation to generation.



*Dr Lorel Colgin –
Cancer Research Unit*

...and from the Laboratory

DNA has come a long way in the last half century. Most people have heard the name, even if they don't quite know what it is. As a child I grew up hearing the term in science fiction, but only later came to understand that it was just a simple chemical, yet one that can hold all the information required for life.

An understanding of DNA is what has caused the current explosion in biomedical research. As a cancer researcher, my own work would be inconceivable without the ability to use recombinant DNA and related technologies to sift through the complexity of human cells to find the genes and factors involved in cancer. The discovery of DNA has affected countless other fields as well. DNA fingerprinting is a celebrity in forensic science, while genetically modified food is an area of extreme controversy, and the direct result of advances in DNA technology.

DNA carries the recipes for life. Yet, with all we have learned about DNA, we now know that this knowledge is not enough. With the sequencing of the human and mouse genomes complete, we realize that there is too much information and not enough understanding. Sequencing the genome has identified thousands of new genes but with no clue as to their function. With current technologies, we are able to detect hundreds of changes in gene activity during cancer progression, for example. Yet, it is difficult to determine which changes are important causes of cancer and which are merely secondary symptoms. New methods are required to map the complex interactions that occur within and between cells, tissues and organs if we are to cure disease, prevent cancer and delay ageing. Nevertheless, this Age of DNA has at least made us confident. Most of us believe that we will triumph over cancer and disease, that there are solutions to our problems, and that we will find them.

Dr Lorel Colgin - Cancer Researcher

"A scientist of boundless energy and enthusiasm"

This is something that we at the CMRI already knew, but now, in recognition of that and his "outstanding contribution to neuroscience", Dr Phil Robinson, Head of the Cell Signalling Unit, has been promoted to Senior Principal Research Fellow by the National Health and Medical Research Council.

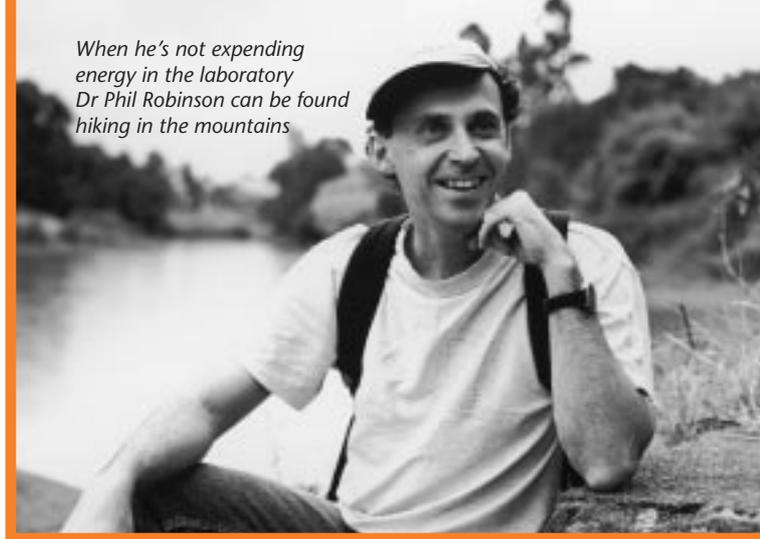
The five year appointment brings CMRI's total of laboratory Heads placed at the highest level of academic achievement in the country to three. Dr Patrick Tam holds the same position from the NHMRC and Dr Roger Reddel has the equivalent appointment from the Cancer Council of Australia.

"This NHMRC appointment is an acknowledgement from my peers of my contribution and standing," said Dr Robinson. "It also increases the attention and prestige given to our laboratory. Students now see this as the international lab of choice for neuroscience."

...with an **NHMRC Project Grant to match**

Now Dr Robinson's energy and enthusiasm will carry him and his colleagues in the Cell Signalling Unit into an exciting new project that was also funded by the NHMRC in its latest round of grants.

When he's not expending energy in the laboratory Dr Phil Robinson can be found hiking in the mountains



The three year Project Grant was awarded jointly to Dr Robinson and Dr Adam McCluskey in the Department of Chemistry, University of Newcastle. The two teams will join forces to develop new drugs to inhibit the protein dynamin.

Dynamin, discovered by Dr Robinson, is a key component in the machinery that enables communication between neurons in the brain.

"We have already found the first drugs that can inhibit the action of dynamin," said Dr Robinson, "Now we can really start exploring this avenue to improve the potency and specificity of these drugs."

Initially the drugs will be used as research tools to further investigate the function of dynamin. Ultimately, they hold the potential to treat brain disorders that result from disturbances in communication across the brain's synapses, such as epilepsy, schizophrenia and Alzheimer's disease.

"The joint nature of this project I think is really exciting," says Dr Robinson, "the chance for biologists and chemists to really work together to reach a common goal will be really interesting and productive."

NHMRC see MusTRD as a "hot" research topic



Dr Edna Hardeman with MusTRD team member Dr Stephen Palmer

Dr Edna Hardeman and her team in the Muscle Development Unit are also recipients of an NHMRC Project Grant which secures the team's position to follow through on a key discovery that has major implications for many muscle diseases including a childhood genetic disorder called Williams-Beuren syndrome.

Four years ago, the team identified an entirely new protein called MusTRD (its unusual name relates to its muscle origin and the codename of a protein to which it is related). They now have growing evidence that MusTRD operates a molecular switch diverting muscle fibre development towards either the 'fast' or 'slow' fibre type by switching different genes on or off. It is the first protein described that can do this.

Fast twitch muscle fibres are important for rapid, high strength movement but tire easily; slow fibres are fatigue resistant and are important for posture

and duration activities. The correct proportions of slow and fast fibres are essential for normal body function. Disruption of this balance frequently contributes to a wide variety of muscle diseases.

The team is particularly interested in Williams-Beuren (or Williams) syndrome (WBS), a developmental disorder that causes many physical problems, cardiovascular symptoms being the major ones. It also causes problems with muscle development.

Children with WBS are missing a small portion of chromosome 7 that contains up to sixteen different genes. This makes it very hard to find out which genes cause which symptoms. Interestingly, the MusTRD gene turned out to be one of the genes missing in WBS. With the help of the NHMRC grant Dr Hardeman's team will be investigating the possibility that a lack of MusTRD may lie at the root of the muscle symptoms in WBS.



NHMRC Peter Doherty Fellows
Dr Amanda Nouwens
(standing) and Dr Ying Cào

CMRI's young Talent also recognized

In another clear indicator of the calibre of scientists employed at CMRI two of the twelve NHMRC Peter Doherty Fellowships granted Australia-wide this year have come to fledgling post-doctoral scientists Dr Amanda Nouwens of the CMRI Cell Biology Unit and Dr Ying Cào of the Cancer Research Unit.

The Peter Doherty Fellowships are designed to encourage young scientists of "outstanding ability" to make research a career and to continue their research training within Australia.

The NHMRC Fellowships will support Amanda and Ying over the next four years as they work on aspects of telomere biology. While Ying is studying the proteins that interact with the telomere DNA at the ends of chromosomes to wrap it into a protective cap, Amanda is looking at the mechanism of the telomerase enzyme, which causes telomeres to elongate, allowing uncontrolled proliferation of cancer cells.

Christian Toouli, a PhD student in the Cancer Research Unit, received a Genentech Scholar in Training award to present his research findings at the American Association for Cancer Research conference on telomeres and telomerase held in San Francisco in December 2002.

You make our day Jeans for Genes® Friday August 1

Plans for the 2003 campaign are well underway. It is our 10th anniversary and we are looking forward to celebrating this milestone. To commemorate, we are holding a Retrospective Exhibition featuring painted celebrity jeans that have been purchased at The Annual Jeans for Genes Art Auction over the last ten years. You can view the exhibition during July at either The Victorian Arts Centre or the Sydney Town Hall and the Sydney Opera House. In conjunction with the Retrospective Exhibition we will hold our Dinner Auction at Dockside, Cockle Bay Wharf, Sydney on 24 July. So put it in your diary now!

Gene's Jeans for Jeans for Genes

When we heard through the grapevine that legendary performer Gene Simmons, from rock group KISS and most recently a highly popular motivational speaker, was in Australia, we jumped at the opportunity of securing Gene's Jeans for Jeans for Genes.

Australian artist Garry Fleming generously donated his talents and painted an amazing portrait on Gene's jeans. Garry recently met the amazing performer and witnessed his wild ways first hand.



Artist Garry Fleming puts a final lick of paint on Gene Simmons' jeans.

Help make our Day!

We are hoping that 2003 will be the most memorable and biggest Jeans for Genes Day in history. We are aiming to raise over \$4 million and we need your help to do it. We are currently looking for corporate sponsors and community Genies.

If you are interested send an email to: genie@jeans4genes.com.au or phone 02 9687 2800.

Protein detective

The recent completion of an exciting upgrade of CMRI's state-of-the-art protein analysis facility means no stone will go unturned in the hunt for key proteins involved in human biology and disease.

Stage one of the facility, the MALDI-TOF mass spectrometer, was installed in May 2001. Stage two saw the delivery of the new QSTAR mass spectrometer, one of only three in Australia, in January 2003. The two machines will provide complementary information to identify unknown proteins.

The QSTAR is also exquisitely sensitive and can obtain data from incredibly small samples of protein.

This facility, only possible through the generosity of CMRI supporters, enables CMRI and their colleagues in the Westmead Research Hub to make a major contribution to worldwide efforts in deciphering our genetic code and the protein components that constitute the working parts of the human machine.

From the young to the old

The beauty of basic research is that its findings can lead us in many directions. And in the case of Dr Lily Huschtscha's work it has lead her from a hunt for the genes involved in cancer to the fundamental mechanisms of ageing. Dr Huschtscha has been awarded an NHMRC Healthy Ageing Research Grant to pursue a group of 'immortal' cancer-like cells, unique to CMRI, that may be hiding some key genes central to ageing. The NHMRC recognised the value of this unique resource in approving the grant application, one of only eight funded out of a total of 80 submissions. Dr Huschtscha will be collaborating with scientists in Canberra and the United States to use the latest genetic and protein analysis tools to identify the genes.



Clockwise from top left:
 Bernice Ole of the NSW Floral Art Club at the Hills Committee's 'Glenhope' event with her 'Christmas Morning' artwork.
 Treasury of Crafts member Carolyn Tranter with her stall of treasures.
 An outstanding "outback" success for the Northern Beaches (née Allambie) Committee's prize-winning Christmas card stall at Warringah Mall: left to right Pat Cox, Lenore Horton and Rowena Graham.
 Behind the aprons (left to right) are Jan Madigan, Lisa Heinz, Janet Buxton and Liz Butterworth of the Vaucluse Committee selling Christmas cards at Paddington Market.



Committee Power

Welcome Adelaide! – new committee

One South Australian Jeans for Genes® Day Genie's enthusiasm for the cause has bubbled over into a commitment to set up an Adelaide Committee. Kate Attard has mustered a team of equally enthusiastic friends and ideas for events are already coming thick and fast. Welcome to CMRI's network of wonderful supporters.

Different name, same committee

To reflect their spreading membership and greater scope of the Allambie Committee's activities, the Committee have decided to change their name to Northern Beaches. We know that their commitment, drive and enthusiasm will continue unchanged.

Tamworth Committee

People from far-and-wide came to Tamworth's Carols for a Cause to exercise their voices and be entertained by The Little Maestros and local talents the Combined School Septet, Ben Hazell and Aleyce Simmonds and the Tamworth High Concert Band.

Scone Committee

The Scone ladies have had a fun time putting together a 2003 Calendar called 'Head of the Hunter Men'. Photographer Howard Archibold was commissioned to take some very 'candid' shots of men in the Upper Hunter region, NSW. We have no doubts they will sell like hotcakes!

Hills Committee

The Hills Committee and the NSW Floral Art Club made the perfect team and created a festive extravaganza at historic 'Glenhope' with Christmas-themed flower arrangements. The Maroota Committee completed the teamwork by serving up delicious homemade refreshments.

Supporters are everywhere

Many thanks to Mrs Pam Witner, a tireless charity worker, who chose CMRI as the beneficiary of her annual luncheon. A delightful lunch was enjoyed by her many friends including members of our Becroft Committee.

Treasury of Crafts

Treasury of Crafts members, from the Hills region of Sydney, have been using their talents for many years to raise funds for CMRI. To date more than \$40,000 has been donated from the proceeds of their regular craft fairs, the latest being their busy pre-Christmas fair, held in North Rocks.

Dates for your Diary

Jazz in the Mountains

At 'Bisley', Mount Wilson.
 Beautiful gardens, homemade food and all that jazz,
 30 March, 11am – 4pm

Strathfield Committee Luncheon

At Didi's in Abbotsford with guest speaker Ita Buttrose,
 5 May

Children's Charity Night

Join the Rotary Club of Cabarita and Strathfield Committee for dinner and entertainment at Le Montage,
 14 March

NSW Police Band Concert for CMRI

Organised by the Judith Hyam Memorial Trust Fund for Cancer. Parramatta Town Hall,
 18 May, 2.30pm, call Diana on (02) 9630 5572

Charity Golf Day for CMRI

At Castle Hill Country Club, organised by the Rotary Club of Glenhaven, 4 March
 Contact Len Gauci on (02) 9899 5561

Vaucluse Committee Tennis Day

Make up a mixed doubles team and enjoy the exciting finals and luncheon at 'Fairwater' overlooking Sydney Harbour, 30 March

Hills Committee Luncheon

Stamford Plaza, Double Bay, with special guests, 5 May

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