

From Professor Nick Martin:

The aim of QIMR's numerous genetic projects is to understand what causes differences between people in their behaviour, habits, and risk of disease. We specifically want to know how important genes and environment are for these differences.

This interest is not just academic. If we can show that a characteristic is largely caused by environmental factors, there is a greater chance that we can identify which aspects of the environment (diet, sun exposure, infections) can be changed to improve it.

If, on the other hand, we show that genes are most important, we have a realistic chance of finding the particular genes involved because of recent breakthroughs in molecular biology. Ultimately this may lead to new and better drug treatments and more effective screening tests.

One very nice thing about working in Australia is that so many people are happy to give their time freely and willingly to help medical research. Receipt of this newsletter indicates that you are one of these and we are grateful.

In trying to cover all projects in so little space, coverage is necessarily brief. If you would like more detail, I encourage you to look at our website, where you will find links to all our research publications.

Thank you for participating in our research and helping make our results possible.

Professor Nick Martin

Genetic & Population Health

**Research Update on Twin & Family Studies at
The Queensland Institute of Medical Research**

What Have We Found So Far?

Melanoma

Queensland has the unfortunate distinction of being the melanoma capital of the world. In 1987 QIMR began the Queensland Familial Melanoma Project to assess genetic and environmental factors in melanoma risk. So far more than 20,000 melanoma patients and their relatives have taken part. We have shown that while sun exposure is the most important factor for most cases, for some families genes are the most important factor. About 1/200 cases come from families where there is a mutation in a gene called p16 which causes melanoma.

In about another 10% of families, variation in coloration appears to be an important risk factor. Those who carry variants in a gene called MC1R that causes red hair are at highest risk. There are other genetic influences on melanoma risk still to be found and which will help in prevention and treatment. But meanwhile, keep up the Slip [on a shirt], Slop [on some sunscreen], and Slap [on a hat] !



Prof. Nick Martin counts the moles on 12 year old twins

Twin Mole Study

This study, in progress since 1992, looks at number and distribution of moles. This is important because a high density of moles is a high risk factor for melanoma. (Other risk factors include high sun exposure, fair coloring, and freckling). So far, more than 600 twin families have taken part. We have found that the number of moles on individuals varies enormously from almost zero to over 300. Identical twins have almost the same number of moles but non-identical twins are much less similar in both number and positioning of moles. This suggests moliness is strongly influenced by genes, although sun exposure is also a major factor.

We are now using genetic linkage mapping to search for these genes.

Photo by Bob Fenney, The Courier-Mail



Premier Peter Beattie donates his DNA to QIMR's Anne Eldridge. Premier Beattie's twin sons have been involved in QIMR research since they were 12.

So far a region on chromosome 9 has been found to account for 33% of the genetic variance in mole count, although this is not necessarily the only cause. A genome-wide scan is now underway to detect other genes which cause melanoma.

To read more about our work and obtain research papers visit our web site: <http://genepi.qimr.edu.au>

One of our major interests for many years has been the role of genes in drinking and smoking. Previous studies have shown that genes influence alcohol dependence in men. Our results show that genes also influence alcohol problems in women - the risk is higher for women with depression. It is also higher for those who have no religious affiliation and for younger women. Evidence from regular smokers shows that those who start smoking daily at an early age are more likely to have more severe nicotine withdrawal than those who start smoking regularly when they are older. There is a close association between alcohol dependence and severity of nicotine withdrawal. We found that 59% of smokers who had severe nicotine withdrawal also had a history of alcohol dependence.

Memory, Attention, and Problem Solving

Most twins from the Twin Mole Study also come back at age 16 to participate in the Memory, Attention, and Problem Solving (MAPS) Study, which began in 1996. We also recruit new 16 year old identical and non-identical twins and their siblings. We are examining brain function and how people vary in the way they deal with the large amount of information they are exposed to each day. The speed with which information is processed varies between individuals, as do the number and types of strategies used. Nearly 350 twin pairs and 80 of their siblings have completed several computerised tasks, had their brain waves measured, and given a blood sample. Parents have also donated a blood sample. The aim is to find genes responsible for different aspects of brain function. We are very grateful to these families for their time and willingness to help with our research.



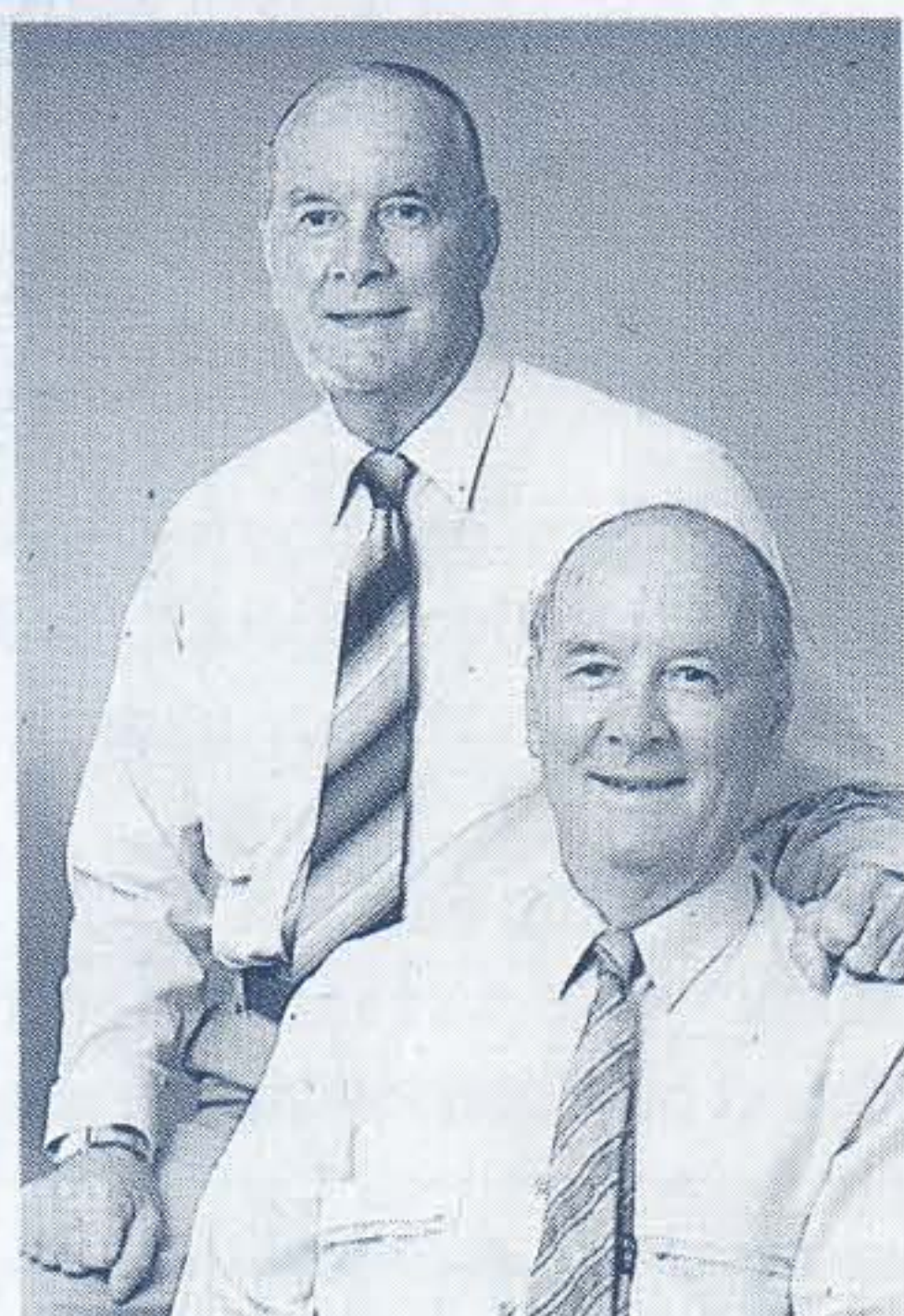
Rowan and Martin teKloot involved in brain function testing

Anxiety & Depression

Over the past 20 years, through interviews about personality and feelings, we have strong evidence of genetic factors in anxiety and depression. Nearly 400 identical twins, 1128 non-identical twins and 1116 of their brothers and sisters took part in interviews about anxiety and depression. Most also donated a blood sample. Over 1500 parents of twins also donated a blood sample, for which we are especially grateful. Over the next 2 years, we will analyse DNA from the blood samples to look for the genes behind anxiety and depression. We hope our work will lead to better treatments for these conditions.

Asthma

Australia also has the unenviable distinction of having one of the highest rates of asthma in the world. Up to 40% of Australian children have some symptoms of asthma at some stage in their lives. Environmental factors, including house dust mite, household pets, fungal spores and pollen are clearly important. Genetic factors also play a major role. QIMR's Dr David Duffy has actively involved Australian twins and their families in the search for asthma genes. He has shown that rates of asthma are continuing to rise in Australia. Already, genes that affect response to medication have been found. The genes actually causing the disease may be isolated in the next few years.



Twins are vital for familial and genetic research



DZ Twinning & Fertility

The most common question we are asked is, "My mother [or sister, or maternal aunt, or grandmother] had twins; what is the chance of me having twins too?" Natural multiple pregnancy in women leading to dizygotic/non-identical (DZ) twins tends to run in families. However, nobody has ever found the genes responsible. We have now found 361 pairs of sisters who have had DZ twins. Another 400 individual mothers of non-identical twins and their parents have joined our study. If we can find the gene(s) responsible for DZ twinning, we will be able to answer that common question. We may also find new ways to control fertility and infertility in women. Analysis of our data so far shows that genes for twinning are on different chromosomes from those in other species. If you would like to take part in this study, please free call Barbara Haddon on 1800 632 576.



Sisters, Sally Tyler (with her twins Nicholas and Lucy) and Jennifer Boulter (with her twins Suzannah and Cameron).

New Studies for the New Century

QIMR has two new studies on the drawing board:

Twin Mothers and their Children (MATCH study)

We want to learn more about problems faced by adolescents and young adults in Australia today. To do this we are interviewing twins who are mothers of children aged 13-21. We are also interviewing these children themselves (with their mother's permission) to understand problems and issues from their perspective. If you are a mother, or if your twin sister is a mother you may receive a letter from us about the "MATCH" study.

Smoking

We are interested in understanding why people become smokers. We also would like to know why some become heavy long-term smokers but others quit successfully. If our funding application is successful we will be inviting twins and their families to take part in this new study of smoking. This study will involve a telephone interview and donation of a blood sample.

Diabetes

Diabetes affects how the body uses food to make energy. People with diabetes may have a reduced life-span, and eye, heart and kidney problems. These problems develop due to complex genetic and environmental interactions, which, through the twin study, we are hoping to clarify. This study is almost finished with 360 twins having completed their interviews. The data are now being analysed by Julianne Condon.

How do you find genes?

By producing genotyping data from purified DNA we look for genetic linkages between a condition/disease and one or more regions of a chromosome.

When a genetic link is found, the next step is finding the exact gene responsible. This is done by using a range of molecular biology techniques including looking directly at the composition of the DNA. It is all time consuming, highly skilled, and very expensive - but we could do nothing at all without your DNA.

Incidentally, identical twins are vital to the earlier stages of our research but when it comes to actually finding the genes, it is non-identical twins and their brother and sisters who are crucial to our success.

If you or your twin have changed address please inform the Australian Twin Registry - 200 Berkeley Street, CARLTON VIC 3053.

Phone: 1800 037 021

Fax: 03 9347 6136

Email: twins@gpph.unimelb.edu.au

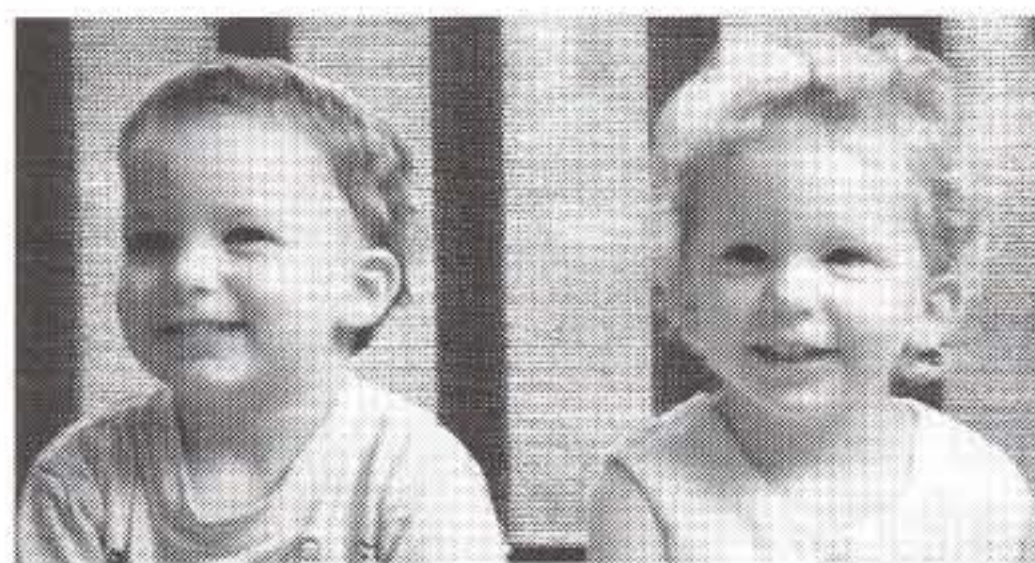
Women's Health

QIMR has found evidence for specific genetic influences on postnatal depression. Although some other researchers have related postnatal depression to emergency obstetric interventions, we found no evidence for this. However, the twin's postnatal depression after her first live birth was associated with the difficulty of the labour.

Dr Treloar also found the same genetic influences continue to effect menstrual symptoms and how much periods interfere in women's lives. We also determined that identical twin sisters were much more similar than their nonidentical counterparts in early cancer detection behaviours, like having Pap smears.



Sisters Rosemary, Michelle and Penny, taking part in QIMR's endometriosis research program.



Alex and Sarah Mackintosh - twins of all ages help research

QIMR - Turning Research into Cures

It is only through donations (all fully tax deductible) from the community that QIMR's 420 scientists can find the cures and new treatments for more than 30 life-threatening diseases.

For information on donations, bequests in wills, research updates or free tours of our laboratories free call 1800 993 000.



Some Frequently Asked Questions

Why do you need blood samples?

To look for genes we need to use DNA and the white cells in blood are the best source of DNA.

What is DNA?

DNA is the information-carrying material that makes up genes. Genes are arranged into larger structures called chromosomes. During foetal development, chromosomes are passed from parent to offspring. By using state-of-the-art laboratory techniques, it is possible to trace this transfer of genetic material (inheritance) within families.

You can play a part in our vital research. Fill in the forms and post with your contribution to:

QIMR, Post Office, RBH, QLD 4029. Phone 1800 993 000. Fax (07) 3362 0111.

Together we CAN make a difference. For tours of our laboratories, call the above number.

☐ Yes, my club, association or organisation would like to have a guest speaker from The Queensland Institute of Medical Research to talk about the latest research and results.

DONATION FORM

Here is my fully tax deductible donation to QIMR

Name: _____

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Post Code: _____ Phone: _____

☐ \$30 ☐ \$50 ☐ \$100 ☐ \$200

Other: _____

Please make cheques payable to QIMR or charge my:

☐ Bankcard ☐ Visa ☐ Mastercard

□ □ □ □ □ □ □ □ □ □ □ □ □ □ □ □

Cardholder's Signature

Expiry Date

BEQUEST/WILL INFORMATION

I would like to make a bequest in my Will to The Queensland Institute of Medical Research.

☐ Please send me a free Wills kit

☐ Please phone me on () _____

to discuss this matter.

☐ I have already provided for QIMR in my will.

Name _____

Address _____

Postcode: _____