



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 more important than environment, 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 details, 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.

Research Update: Genes & Health

Twin & Family Studies at the
Queensland Institute of Medical Research

2005 - 2006

<http://genepi.qimr.edu.au>

1800 257 179 (freecall)

What Have We Found So Far?

Melanoma

One of the key issues faced by researchers is the question of "how much sunlight is required to cause a melanoma?" Scientists have long known that melanomas are different from other types of skin cancer, in that they can occur on parts of the body that don't get very much sunlight. Understanding why this happens and how they might be prevented, is an important aspect of our continuing research. QIMR is now following up families who participated in earlier studies that began in Queensland in the early 1990s. Over 2000 families have been invited to participate in the study, with preliminary findings soon to be published.

Nicotine



We have found that genetic and environmental influences on smoking are different for men and women. Genes influence whether both women and men smoke, but they have a stronger influence on men. Additionally, the family environment influences women's smoking habits, but not men's. We are currently undertaking research to identify the genes that influence smoking habits, and to find out how these genes influence men and women differently.

New Australian study on breast density in women with endometriosis

This new study, funded by the National Health and Medical Research Council, is being conducted jointly by the University of Melbourne's Centre for Genetic Epidemiology and QIMR. From QIMR we will be inviting participants in the Genes Behind Endometriosis study who are in the families with sisters diagnosed with endometriosis and are aged

40-70 years old, for permission to scan a recent mammogram. Endometriosis is a hormonally-influenced condition and women often take hormonal type medications for endometriosis. We know that breast density is a risk factor for breast cancer. Therefore we think it's important to investigate whether breast density differs in women diagnosed

Twining

Why do some families have lots of twins in their family tree? The tendency to have non-identical twins is partly due to the mother's tendency for increased multiple ovulation (releasing 2 or more eggs in a cycle). Our research is focussed on finding out why this happens to some women. **If you and any of your sisters have conceived non-identical twins and would like to participate, from anywhere in Australia, please call our 1800 number. We are keen to talk to you!**



with endometriosis compared with other women, and whether breast density is influenced by genes, as suggested by results of an earlier twin study run by Prof. Hopper and his colleagues. We really hope that women approached will be interested in helping this new study, even by having a mammogram if they previously haven't had one.

Anxiety

The Anxiety study at QIMR is based upon siblings who are extremely similar or dissimilar for Neuroticism on one of several measures of human personality that were originally described by the psychologist Hans Eysenck. The study is aiming to identify genes that cause anxiety and depression and related symptoms and is now running at full steam. The gathering of results is nearing completion and by genotyping twins and other siblings we hope to have a very extensive set of results for analysis in the next few months. Our results will be complemented by a similar study carried out with Dutch twins, enabling us to look for consistency in the locations of genes in the different samples. We have already been able to combine our results concerning the clinical diagnoses of rare conditions related to anxiety and depression (e.g., Panic disorder and Obsessive Compulsive) and show that these are manifestations of genes that confer the symptoms of anxiety and depression. We eagerly await the results of genotyping so that we can get a better idea of what these genes might be.



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. This process is 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 brothers and sisters who are crucial to our success.

Migraine



In a recent genome-wide search for migraine susceptibility genes, in 756 twin families, we found significant evidence for the presence of a migraine gene on chromosome 5 and suggestive evidence for genes on chromosomes 8, 10 and 13. We also replicated previously reported migraine loci on chromosomes 6 and 1, the latter being close to a gene causing a rare and severe form of migraine with aura, potentially implicating this gene (ATP1A2) in familial typical migraine for the first time (paper submitted to the prestigious American Journal of Human Genetics). We are now testing a larger sample of twin families to replicate these exciting findings.

Variation in blood lead

Lead is a potentially toxic environmental chemical, coming from industrial processes, lead-based paint on older houses, and until recently from leaded petrol. The twins in this long-term study on variation in blood lead came from a wide range of locations. We expected that blood lead concentration would be affected by where people live, as well as by the known effects of age, sex, smoking and drinking. However, the obvious predictors of probable lead exposure such as city or country living and socio-economic status did not show significant effects. Analysing the twin pair data by zygosity has now shown that genetic factors are important, at least in adults, and we are hoping to identify the genes involved as our next step.



What is genetics?

Genetics is about differences:

Between animals, trees, bacteria and humans.

Genetics is also about similarities:

Between you and the rest of your family, including your ancestors, between you and other humans and between you and other species.

Genetics is the science of heredity that tries to account for both these similarities and differences.

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. At conception 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.

Some frequently asked questions

If you have changed address or phone number please let us know:

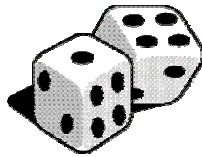


freecall 1800 257 179

or write to:

Genetic Epidemiology QIMR
Post Office Royal Brisbane
Hospital
QLD 4029 Australia

Gambling



Excessive gambling is a major public health problem. We are interested in whether our genes put us at risk for becoming problem gamblers and whether problem gambling is associated with excessive alcohol and tobacco use. So far we've interviewed 2,000 twins and we're planning to interview another 4,000 over the next two years. You may be hearing from us soon!

Alcohol

Drinking habits are partly determined by the genes we inherit. Non-identical twins have drinking habits which are much less similar than the drinking habits of identical twins. This is true even when the twins have been living apart for several years. We previously discovered a variant of a gene called *alcohol dehydrogenase* which appears to protect about 10% of Australians from excessive drinking and developing problems with alcohol.

We are now conducting another major research program to discover other genes which influence drinking habits and risk of alcohol dependence. We have just discovered that variants in another related gene called *aldehyde dehydrogenase* also seem to protect some people from risk of alcoholism. This had previously been shown in Asians but ours is the first evidence that this gene is also important in people of European extraction.

Endometriosis

We have achieved the largest collection of sibling pairs (sisters in our case) for a complex disease that has ever been collected anywhere in the world! In total, we had around 4,000 women with surgically confirmed endometriosis participate in our study. Adding parents and other family members brought the total to around 10,000 people across Australia!

There were 931 families where 2 or more sisters both had endometriosis. We have found two chromosomal regions where sisters were sharing more genetic markers than we would normally expect. We intend to publish these results in a top medical / scientific journal very soon, and are on the way to finding the genes.

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

Twins working on twins at QIMR



Peter Visscher has recently joined QIMR and will involve his twin sons, Luke (left) and Hugo (right), in the mole count study.

Professor Peter Visscher joined the QIMR team in January 2005 from the University of Edinburgh (UK). He visited for a few months in 2003 and was very impressed by the fantastic collection of high quality data that have been collected through the participation of so many twin families. So impressed that he wanted to return to join the team! His 11-year old non-identical twin boys will join the mole count study later this year. The pictures were taken the day after they come off the plane from the UK - it didn't take them long to find Dream World!

Megan Ferguson has been working at QIMR since 2003. Megan is currently a project coordinator for several studies, including an early experiences project and the gambling project. Megan's twin sister, Fenella lives in Rockhampton and is the mother of one - no more twins in the family yet!

Megan Ferguson (right) and her twin sister Fenella (left)

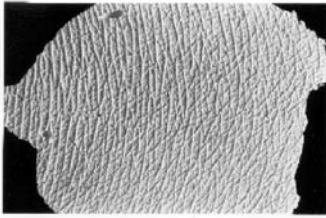


Charles (left) and Will (right) Coventry

Will has been a PhD student at QIMR since 2003. He is exploring the effects

of genetics, the family environment and the individual environment on social support and the parallels with depression. Will is also looking at how the serotonin transporter gene is related to social support and depression in individuals who have and have not experienced traumatic/stressful events in their lives. Will's twin brother, Charles is a grain trader in Sydney.

How we use skin impressions



The fine pattern found on the skin on the back of your hand

The middle layer of our skin changes when we are exposed to sunlight. The level of deterioration is important to determining whether a person might develop skin cancer. Unfortunately examining this layer is expensive and rather unpleasant!

The fine pattern on top of the skin (see picture), deteriorates with age. Is this also due to the sun? If so, then perhaps we can use deterioration of

fine patterning on the skin as an alternative to examining change in the middle layer of the skin or measuring an individual's exposure to sunlight. Using the impressions of the skin gathered so far, we have found that: only 3% of the deterioration in the top layer of the skin is due to sunlight; about 10% is due to skin colour. Interestingly, almost 86% of the variation in skin pattern between teenagers is due to their genes! We are currently searching for these genes.

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

Where do you live? And where would you prefer to live – Tahiti? Manhattan? Back o' Bourke?

Analysis of the addresses of twins participating in QIMR studies has recently given an interesting perspective on where people live. Classifying twins' addresses as urban, suburban or country, and then looking at the similarity of the two members of each twin pair, we found that location has a genetic component which becomes stronger with age. Younger twins (aged about 25 to 30) live where their early life has made them feel at home, but as we get older (aged 45 or more) we have an increasing tendency to act on our own individual preferences. At least in Australia, these preferences have a significant genetic component. It will be interesting to see whether this pattern is general or if there are differences between countries, either by population density or by degree of economic development.

Eczema

This study recruited families with at least two siblings who suffered from eczema. After our campaign in September 2003, we were inundated with eager respondents and now have 563 families taking part – almost double the number we needed! The study is now closed to new participants as we have almost finished the data collection phase. We expect genotyping results to be completed in a few months and look forward to passing on the results to you in the next newsletter.



Update on our Studies of Asthma

At present, asthma affects nearly 2% of the world's population, having earned the status of an epidemic disease. For the past 10 years, our Asthma Research group, led by Dr. David Duffy, has conducted a number of studies that have investigated the genetic basis of asthma. You may even have been involved in one of these studies. Over 3000 twins and relatives from these families provided detailed information on past and current asthma status, and on the level of exposure to known environmental asthma risk factors for asthma, from the time of conception (e.g. maternal smoking during pregnancy), through childhood (e.g. number of respiratory infections as a child), to adulthood (e.g. diet). In addition, most

twin research
and
human genetics

TWIN RESEARCH AND HUMAN GENETICS is the international journal for those seeking an academic review of all manner of research in the field.

Edited by Professor Nick Martin of the Queensland Institute of Medical Research, it covers all areas of human genetics with an emphasis on twin studies, genetic epidemiology, psychiatric and behavioural genetics. Included is research on multiple births in the fields of epidemiology, genetics, endocrinology, fetal pathology, obstetrics and pediatrics.

The journal may be obtained by subscription but is also widely indexed and may be viewed online.

Visit www.ists.qimr.edu.au or contact ists@qimr.edu.au

participants (88%) donated blood which allowed us to extract DNA from white blood cells for our genetic analyses.

To summarise 10 years of research, we have identified four regions of the genome (that is, the genetic material made of DNA) that are very likely to harbour genes that carry a fault (i.e. mutation) in some Australians that increases their risk of developing asthma. Three of these four regions have also been identified by other asthma research groups in the USA, France and Holland. We are currently studying this new region in more detail and we hope to be able to provide you with more information on this new region in subsequent newsletters. Stay tuned!