

Multiple genes for multiple sclerosis

Australian and New Zealand researchers have played a major role in an international collaboration that has brought to 57 the number of known genes which can determine a person's risk of developing MS.

The research, published in the prestigious international journal *Nature* in August 2011, shows that the immune system is fundamental to developing MS.

"Almost all these genes implicated in MS are involved in regulating the immune system. So the research is compelling evidence that the crucial disease mechanism for MS primarily involves a disturbance in the immune system," said A/Prof David Booth from the Westmead Millennium Institute in Sydney who represented the ANZgene team in the International MS Genetics Consortium (IMSGC) Strategy Group.

His colleague Prof Graeme Stewart, a Clinical Immunologist at the Westmead Millennium Institute, was one of five governance members of the IMSGC (with colleagues from Cambridge, Harvard, Yale and UCSF) and a member of the 11 person Project Direction Committee for the *Nature* study.

Prof Stewart said, "Discovering so many new leads is an enormous step towards understanding the cause of MS. Most importantly, for people with MS, these genes also strengthen the case for immunologic treatments currently in clinical trials and point to new therapeutic approaches."

MS Research Australia (MSRA) largely enabled the Antipodean contribution to this discovery by funding and facilitating Australian genetic research into MS from 2007.

"This publication represents the most recent culmination of a very successful international research program that we are extremely proud to have been part of," said Mr Jeremy Wright, Executive Director of MSRA, "and we're very grateful to the many Australians with MS who contributed DNA samples."

"This research is a key part of our goal to accelerate progress towards new treatments and a cure for MS," said Mr Wright. "Our investment in MS genetics in Australia so far is more than \$2.6 million, thanks to contributions from John T. Reid Charitable Trusts, the Trish MS Research Foundation, the Australian Research Council and the National Health & Medical Research Council."

**ANZgene
scientists
in world
discovery**



PROF GRAEME STEWART FROM WESTMEAD MILLENNIUM INSTITUTE REPRESENTED AUSTRALIA IN THE GLOBAL COLLABORATION.

For this latest discovery, ANZgene scientists pooled DNA samples and data together with a total of 23 research groups in 15 countries to conduct a powerful comparison of the entire genomes of 9,772 people with MS and 17,376 people without MS.

The study confirmed 28 genetic variations that had been previously identified and added another 29 variations to the list. The variations confirmed by the study included two which were discovered in 2009 by the ANZgene collaboration. One of these was a vitamin D metabolism gene and the international study has now identified a second vitamin D gene, providing insight into a link between genetic and environmental risk factors.

The genetic 'signature' in people with MS is the same regardless of the gender of the person, the severity of the disease or the type of MS (relapsing-remitting or primary-progressive). However, the study suggests that a person's overall genetic susceptibility may contribute to the age at which their disease becomes apparent.

The challenge now is to uncover the mechanism by which the genes contribute to development of MS and to use this information for the design of new and better treatments.

The genetic testing and statistical analyses for the *Nature* paper were funded by the Wellcome Trust in the UK and the study was led from Cambridge and Oxford Universities. ■

MS research in the 'city of dreaming spires'

In 2009, Dr Julia Morahan was awarded the inaugural Macquarie Group Foundation Australian-UK MS Society Exchange Fellowship – which makes possible her research into the epigenetics of MS at the University of Oxford's renowned Wellcome Trust Centre for Human Genetics. This has given her a unique opportunity to work with Prof George Ebers, one of the world's foremost MS experts.

"Oxford is known for its scientific excellence and it has been a privilege to meet and work with such outstanding scientists," said Dr Morahan. "It has been great for me to have access to the newest technology and ideas that are available here."

Dr Morahan already had an impressive track record in genetic research having previously led the Stacey Motor Neuron Disease (MND) Molecular Biology Laboratory at the University of Sydney. Her expertise in the tools of genetics and molecular biology allowed her to cross easily into the MS field.

Two years into the Fellowship, Dr Morahan's research is progressing exceptionally well with three research papers published just this year. Prof Ebers is enthusiastic about Dr Morahan's contribution. "Her work is at the centre of terrific new developments in the epigenetics of MS. We are delighted to have her working with us."

Unlike the IMSGC research which has identified 57 genes which predispose people to MS (see cover story), Dr Morahan's focus is on the identification of epigenetic changes which lie outside the DNA sequence. These epigenetic changes are generally thought to be involved in regulating whether a gene is switched on or off.

One such mechanism is methylation of DNA – in which a small chemical 'tag' is added to a gene. Methyl tags play a role in silencing genes across tissue types and can be involved in pathological processes. Dr Morahan aims to identify the role of methylation on the genetic region which confers the highest risk of MS: the major histocompatibility complex or MHC class II region.

Identical twins provide an ideal way to study how epigenetic changes affect disease susceptibility, their DNA sequences are identical but can differ in their epigenetic 'tags'.



DR JULIA MORAHAN IS INVESTIGATING THE EPIGENETICS OF MS AT THE UNIVERSITY OF OXFORD.

Prof Ebers is a leading researcher in the Canadian Collaborative Project on Genetic Susceptibility to Multiple Sclerosis. As part of this project, large numbers of twin pairs have been identified in which both have MS or only one has MS (discordant).

"Working with such a well established cohort of patient samples has allowed us to detect some interesting differences in the discordant twin pairs, particularly at two locations within the MHC class II gene region," said Dr Morahan. "I now need to study the functional impact of these changes to establish how they might affect gene regulation and the development of MS."

Her obvious dedication and excellent progress in the laboratory has not stopped Dr Morahan from enjoying the beauty and history of the 'city of dreaming spires'.

"I am very grateful to both MSRA and the MS Society of UK for giving me this opportunity. It has been very constructive to experience the international nature of science."



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F5m⁺
Foundation 5 Million Plus

F5m+ is a new beginning; and you are all invited to be a part of it.

Dear F5m+ ers

Foundation Five Million (F5m), was the dream of my husband, Ian Ballard. He developed the idea and it grew to a concept, which launched in November 2005. After countless fundraising events, it became a reality when we hit the target of \$5million in May 2011. Every cent is for research to find a CURE for multiple sclerosis

You might have followed our journey through Next or our website, and seen some photos or read a story of FUNdraising events. Whether it was 12 year old Alex, who held a cake stall and raised \$140, a group of 40 plus school mates who raised \$200,000 in the Gong ride, you may be aware of an Everyday Hero or a GoFundraiser or perhaps you have heard of Katrina, the wife of a person with MS, who walked from Mudgee to Sydney and raised nearly \$150,000. Or perhaps you, too, have been a fundraiser? I am sure you will agree all fundraisers are amazing and should take a bow.

When Ian was diagnosed with MS in 1994, we were devastated. We should have been over the moon because we had just had our third child. But, as time passed, our grief at his diagnosis turned to relief. This might sound strange but we started to think, "our children will know their Dad". Ian would get to see his kids grow up and if we were lucky enough, Ian would be able to walk his daughter down the aisle. Unfortunately, Ian wasn't that lucky, but he did leave his family and friends a pathway to make a difference in F5m.

F5m has enabled people who are affected by MS, to gain some control. We have open meetings on the second Wednesday of the month at the MS office in Chatswood NSW, where we share a glass of wine, (ok a bottle!) and bounce around ideas of what our next fundraising event will be. We are all amateurs – whose previous fundraising experience was turning a couple of sausages on a BBQ or selling a box of chocolates to work colleagues. But we set our sights high and encouraged each other and here we are – with \$5 million!!!

So now we have hit the \$5 million mark, where to now? How do we top that? After much discussion, (well, 15 minutes), we are moving onwards and upwards! Hence the groups new name F5m+ and a chance for all of us to be involved in finding THE CURE. We believe that the last few years' developments in research have brought us so close we can almost smell it.

While we are proud of our achievement, it has only been possible through the unwavering support of MSRA, in particular the MSRA board, Jeremy Wright MSRA Executive Director and the one and only Neil Robertson F5m+ Campaign Manager. Not one event or function would have been possible without Neil's support. His dedication to F5m has been a huge part of our success.

Since our launch, we have had Australia-wide support and we now even boast events in Europe. Not only have we raised money and found unimaginable friendships, we HAVE made a difference So please know your support has never been taken for granted, in fact it has inspired us to keep going.

F5m+ is a new beginning; and you are all invited to be a part of it.

Forever grateful

KBallard

Katie Ballard
F5m+ Patron

Wilder about fundraising

Chris Wilder admits it has taken a while to recover from the North Face 100km trail ultra-marathon on May 14 – an effort which raised a fabulous \$5,710 for F5m+ and MS research.

Despite running against 800 competitors through the NSW Blue Mountains – Chris already has his sights set on further fundraising.

"If I managed to raise over \$5,000 through a nice run in the Blue Mountains, there is huge potential for MS to get more support and recognition through individual efforts," Chris said.

"I loved the event. It was, without a doubt, the hardest thing I've ever done," said Chris who had not run further than 45km in training.

He was thrilled with his time of 14 hours 37 minutes. The North Face was Chris's first ultra-marathon and he had aimed for a sub-17 hour time for the race. ■



Photo: Aurora Images.

F5m+ ensuring the best research projects will be funded



F5m⁺
Foundation 5 Million Plus

F5m+'s goal is to raise funds for research into MS. With over \$5 million raised so far, it is now time to decide how to allocate that money to ensure that the best projects are funded now and in the future. Exciting times indeed!

MSRA has formally established a Board Sub-committee known as the F5m+ Funds Allocation Sub-committee, in order to consider projects which have been recommended by MSRA's Research Management Council and to decide which projects will receive existing F5m+ funds.

For prospective fundraising, we are proposing to select two recommended projects per year for F5m+ers to fundraise for – so you can decide for the purposes of your event advertising which of the two projects you will focus on. The funds would be earmarked until we reach the amount needed to fund the project. Of course, you don't have to nominate any project and can leave the allocation to the Sub-committee, if you wish.

Sub-committee members, who will be appointed by the MSRA Board, must either be F5m+ fundraisers or people who have otherwise had meaningful participation in F5m+. To make sure we are kept up to date on proposed research projects, a member of the Sub-committee will attend the meetings of the Research Management Committee as an observer to provide feedback to the Sub-committee.

The inaugural co-chairs are founding F5m+ members Mike Hemingway and Sarah Ross-Smith.

The Sub-committee will provide reports back to the MS community, so you know where those hard earned dollars are being directed – and to learn more about the selected projects and researchers.

In order to help the Sub-committee make these decisions we want your help. We are proposing that we will have an annual

survey of the F5m+ community so that we can understand the areas of research the F5m+ community wishes to fund in broad terms.

But right now, we would like to hear your suggestions on:

1. the makeup of the Sub committee and its processes;
2. in general terms the areas you think should be funded out of the following MSRA research categories;
 - Prevention Research – looking at the environmental influences of MS (Vitamin D/EBV)
 - Prevention Research – MS genetics studies – investigating the mechanisms and potential diagnosis of MS
 - Neuropathology – research into the 'cause' of MS via human MS tissue research
 - Neuropathology – repair and regeneration – the 'cure' of cells damaged by MS

Your suggestions should be sent to: F5m+, PO Box 1246, Chatswood, NSW 2057 ■

Upcoming Events

11 SEPTEMBER	Bridge to Brisbane
18 SEPTEMBER	City to Bay, Adelaide
18 SEPTEMBER	Blackmores Running Festival, Sydney
29 SEPTEMBER	Throw the Book, Paddington
06 NOVEMBER	Run 4 Fun, Sydney
13 NOVEMBER	City 2 Sea, Melbourne
18 NOVEMBER	Leura Golf Day, NSW

For more information visit www.F5mplus.org.au
or call 1300 356 467

Top five FAQs at the MSRA Brain Bank



Registering more than 610 donors has made the MS Research Australia Brain Bank aware that many people with MS (PwMS) and their families have similar questions and concerns before deciding to register as a brain donor.

Much of the MS research in Australia depends on the use of human tissue, donated by PwMS committed to helping others even after their death. Choosing to register as a brain donor is a wonderful legacy, yet it is not a decision to take lightly. It is essential to discuss the registration and donation process with your family members to ensure you have their full support and understanding.

These are the most commonly asked questions by those considering to register as a brain donor:

I'm already an organ donor. Do I need to register again as a brain donor?

Yes. You are not automatically a brain donor if you are a registered organ donor. Brain donation for research requires separate consent.

You can register as both an organ donor and a brain donor. To become a brain donor for MS research, please register with the MSRA Brain Bank and you will be sent further information and a state-specific consent form to complete.

Does it cost me anything to donate tissue?

No. The MSRA Brain Bank assumes all financial responsibilities for tissue collection, including transportation fees and the cost of neuropathological examination.

Find an MS trial on our improved website

For some people with MS, especially those not responding to currently available therapies, clinical trials can offer early access to alternative treatments. Participating in trials and research also gives people with MS the chance to contribute to Australian research towards better treatments and a cure.

The MSRA Clinical Trials Network (MSRA CTN) is committed to improving both patients' and neurologists' opportunities to participate in trials. As part of this commitment, the MSRA CTN website aims to provide up-to-date information and resources. The site has just undergone a complete overhaul and the refreshed site is now live.



Do I need to write in my will that I am a brain donor?

No, you do not need to mention that you are a brain donor in your will. The brain donor consent form is sufficient for brain donation. The most important thing to ensure brain donation is that your family is aware and supportive of your wish, and that they understand the MSRA Brain Bank should be notified of a donor's death as soon as possible.

What if I change my mind after registering as a brain donor?

You may withdraw your consent to donate your brain at any time by returning the Withdrawal of Consent Form (in your brain donor Information and Consent Pack). Furthermore, we will always respect your family's wishes if they refuse or withdraw consent for brain donation at the time of death, regardless of your own pre-consent.

Will brain donation affect my funeral arrangements?

No, brain donation is organised and performed as rapidly as possible after death and would not delay or interfere with the normal course of events associated with a funeral, cremation or burial. The donation procedure does not affect the ability to have a viewing or open casket.

We are always glad to answer any questions or discuss any concerns so that you can make a well-informed decision. Please phone **1300 672 265** or email msrabrainbank@med.usyd.edu.au or visit our new website: www.msbrainbank.org.au



The site contains information on

- what's involved in participating in a clinical trial
- a state-by-state listing of ethics-approved, current clinical trials for MS in Australia and New Zealand, and
- links to further resources.

We believe this site provides a valuable addition to the arsenal of reliable resources available to support people living with MS and we welcome your feedback.

Anyone interested in participating in a clinical trial should always speak to their treating doctor before volunteering for a trial.

Visit the new MSRA Clinical Trials Network website: www.mstrials.org.au

Broken Hill Family Fun Day

Community support is vital for both raising awareness and funds for MS research. At MSRA we are lucky to have a veritable army of supporters from all around the country to help achieve these goals.



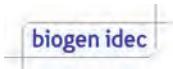
A FIRE BRIGADE DISPLAY, FACE PAINTING AND A RAFFLE ALL CONTRIBUTED TO THE FUNDS RAISED AT BROKEN HILL.

On Sunday 17 July it was the turn of a passionate group of fundraisers in Broken Hill, who organised a Family Fun Day in their local park to support MSRA. These supporters – from local radio stations 2BH and Hill FM – raised \$1,368 to help us in our search for a cause and a cure.

Local bands, a sausage sizzle, face-painting and a display from the local fire brigade made up the day's entertainment. MS Ambassador Mark Slade gave a heartfelt speech about his experience of MS. The day was a great success and came to an end just in time to see the rain begin!

If you would like to find out more about supporting MSRA through your local community please contact the MSRA office at info@msra.org.au

MSRA Partners



Blake Dawson



Yes, I want to help MS Research Australia

Mail this form or donate online www.msra.org.au Donations over \$2 are tax deductible

My one off tax deductible donation is \$ _____

I want to support MSRA on an ongoing basis.

please charge \$ _____ to my credit card per month until notified.

Please debit my: Visa Card Mastercard Amex

Card No: _____

Exp: _____ / _____ Signature: _____

OR I have enclosed my: Cheque/Money Order payable to MS Research Australia.

Title: _____ First Name: _____ Surname: _____

Address: _____

Suburb: _____ Postcode: _____

Telephone (W): _____ (H): _____

Email: _____

Please note here if your donation is made in memory of someone or for a function.

name of person / function name:

Please send me information on how I may support MSRA in my Will.

Check this box if you do not wish to receive future updates from MSRA



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