

Good news for MS genetics research... and Australian science

The international search to unravel the complex genetic factors of Multiple Sclerosis, has resulted in an exciting discovery being announced recently.

Australian scientists played a significant role in leading to this finding of a second MS gene, the results of which were published simultaneously in prestigious scientific and medical journals – *The New England Journal of Medicine (NEJM)* and *Nature Genetics*.

Each publication pointed to a genetic association with a protein essential to the regulation of proper immune function, the interleukin-7 receptor (IL-7R). The definitive nature of the researchers' findings points to a critical role for IL-7R in MS and provides great impetus for further studies on this association. In *NEJM*, the paper was afforded the rare distinction of being accompanied by an editorial. *Nature Genetics* published two papers simultaneously on IL-7R, one from the USA/UK and one from Scandinavia.

Combined, these research papers involved testing the DNA of over 20,000 people in experiments made possible by international collaborations, the mapping of the human genome, remarkable advances in 'rapid throughput' genetic testing and significant funding by governments and other agencies.

Australian science takes pride in this milestone discovery. The world was first alerted to the role of IL-7R in MS in 2003 by a team led by Prof Graeme Stewart and Dr David Booth at the Westmead Millennium Institute, Westmead Hospital. This Sydney team has been concentrating on IL-7R ever since. Prof Stewart is a board member of Multiple Sclerosis Research Australia (MSRA) and director of Westmead Hospital's Institute for Immunology and Allergy Research. He also contributed to finding the first MS gene (HLA) which was found in the 1970s, when he was a PhD student.

'It took the size (and funding) of the overseas experiments however, and confirmation by results in multiple countries, to make this finding internationally accepted,' said Prof Stewart. 'This provides the potential, that will take several years to realise, of better treatments for the many people who live with this dreadful disease and who are long overdue for more effective therapy.'

How might IL-7R be contributing to the cause of MS? It is an essential molecule for the proper function of the immune system's protagonists, the T-cells. These are important in the elimination of intruders in the body and have long been identified as an important player in MS. The genetic findings will quicken the pace of searching for the exact role played by IL-7R and through this, will direct new approaches to the development of effective treatments.



► PROFESSOR GRAEME STEWART ... HAPPY WITH RESULTS.

The next step – Australian Gene Mapping:

Meanwhile, in Australia, no less than eight research institutes, coordinated by the University of Melbourne and the Westmead team, are currently collaborating in the biggest Australian genetic experiment ever for any disease. When linked with the overseas MS studies, the international collaboration will be the most comprehensive study ever on MS.

This project recently received a special linkage grant from the Department of Education, Science and Training via the Australian Research Council (ARC). It has matched the amount offered via the research facilitator MSRA, to establish a budget now of over A\$1mill. Significant support has come from the John T Reid Charitable Trusts and the Trish MS Research Foundation.

The researchers will have access to the MS Gene Bank, another of MSRA's research initiatives, which has already collected more than 2,600 blood samples and MS patient profiles. The MS Gene Bank's collaborators (together with Melbourne and Westmead) include Flinders University, the University of Tasmania's Menzies Institute, the University of Queensland, Griffith University, the University of Newcastle and the University of Western Australia.

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The next step

The project's kick-start is well-timed, according to Jeremy Wright, Executive Director of MSRA. 'Advances in technology will enable us to do genetic testing on a large scale for Australia and do it economically. Also the team has close links with the international MS genetic research consortium based in Cambridge University. So now with this funding, we're in a position to directly compare the Australian results with the international studies.'

Professor Graeme Stewart said the project is 'the best chance we've ever had for discovering new genetic factors in the causes of MS. It's also possible that different genetic factors are at work in MS in Australia and we can only discover those by comparing results from elsewhere'.

A major difference between the newly funded Australian study and international research is Australia's focus on different forms of MS such as relapsing-remitting MS or the more aggressive primary-progressive MS. The MS Gene Bank's robust sample profiling has made this possible.

'We're looking for genes which cause the disease and influence the clinical course and severity or rate of progression. No one else is looking at these nuances,' said Professor Stewart. 'New knowledge from this gene mapping project will also benefit other areas of MS research including epidemiology, immunology and neurobiology.'

If the Australian and international research continues on a successful path, the real winners will be people living with MS.



▶ PROFESSOR TREVOR KILPATRICK AT THE MS FRONTIERS CONFERENCE, LONDON.

UK Research Conference

MSRA partnered a major MS research conference in London on June 12th – 14th, hosted by the MS Society of UK and co-partnered by the National Society for MS (USA) and the MS Society of Canada. The Australian participation was sponsored by our generous corporate partners Macquarie Bank Foundation and Bayer Schering.

Three representatives attended for MSRA, Prof Trevor Kilpatrick from Melbourne University, Dr Bill Carroll, who is chairman of MSRA's Research Committees and Jeremy Wright, MSRA's Executive Director. MS NSW/VIC was also represented by Elizabeth Boros, who attended in her professional capacity as a physiotherapist.

Australia's recent emphasis on epidemiology was outlined by Prof Trevor Kilpatrick in his presentation. Trevor featured the Ausimmune Study and its potential to highlight the link between Vitamin D and MS. Other speakers emphasised the need for human tissue research and the limitation of animal models.

The potential for significant collaboration between UK and Australian researchers was also discussed with the MS Society of UK. There is a proposal for an award that might augment this collaboration.

Staying on the treadmill...

Story by: Liz Boros Physiotherapist
MS Society of NSW/VIC, Blackburn

The MS Frontiers Conference in London, in June was a fantastic opportunity to meet other physiotherapists from the MS Society in the UK and to hear presentations on physio for people with Multiple Sclerosis.

The conference did much to highlight the many benefits of exercise as well as reveal the latest in MS research throughout the world. A paper by Dr. Helen Dawes (Senior Lecturer in Exercise Physiology and Associate Research Fellow at the Department of Clinical Neurology, University of Oxford), was on research with treadmill exercise for people with MS. It was a 4 week program on an aerobic treadmill, 3 times a week and 30 minutes each session, and showed that the exercising group improved endurance over two minutes plus increased walking speed demonstrating significant benefits for people with MS.

Another presentation by Carolyn Young, the Neurologist and Medical Director of the Motor Neurone Disease Centre at the Walton Centre in Liverpool, showed the benefits of rehabilitation for people with MS.

A number of articles were presented as supporting evidence about the advantages of rehabilitation Freeman 1997; Patti et al 2002; Craig et al 2002 and Petajan 1996. The conclusion was that exercise, as part of this rehabilitation, is not only helpful but essential for people with Multiple Sclerosis.



▶ MELBOURNE PHYSIOTHERAPIST, LIZ BOROS.

PRESENTATIONS invited...

Scientific meeting on 'Progress in Multiple Sclerosis Research'

The ninth biennial scientific meeting on 'Progress in Multiple Sclerosis Research' will be held in Melbourne at the Walter & Eliza Hall Institute of Medical Research 15-16 November this year. Contact Sue Barham if you would like to present your abstract. Phone (08) 9346 2471 or Email:sumsr@iinet.net.au



▶ ESTHER ALTHAUS AND FIONA HALL AT MELBOURNE LAUNCH OF ON SHAKY GROUND, AN MS EPISODE IN ANTARCTICA.

How F5m made its first million

The F5m team and its many supporters are celebrating – and deserve congratulations. The network – which supports people with MS who are helping themselves by raising funds – has raised its first million dollars for research into MS in just over 18 months!

And, spurred on by their success, F5m has set their next target, \$2 million to be raised in an even shorter time – by June 2008.

'It's possible because F5m has grown. More people are involved from all over Australia,' said Ian Ballard who founded F5m. 'We get calls all the time from people now wanting to fundraise so the MS Community is aware, willing and motivated.'

'With July's breakthrough news about an MS gene being identified, research may be even more productive so the more resources put to investigating MS – the better.'

F5m's coffers hit the million mark in early July when contributions came from events around Australia, even overseas. Rebecca Maxwell, a Singapore-based Victorian woman walked 850 kilometres across Spain to raise nearly \$4,000; in Melbourne 'On Shaky Ground', an exhibition of photographs in Antarctica, by Fiona Hall and Stellar Fraser raised some \$10,000 and Rob Williams went to picnic race day at Esk in QLD and raised over \$2,500. Then there was the wonderful 'Making Smiles for MS' dinner organised by students from Kenvale Tourism and Hospitality college which raised \$12,000.

June Trivia Month was a fantastic success with a handful of different themes such as books, music and 'crazy trivia' (even including karaoke clues and answers). Together they pulled in about \$40,000. Mike Hemingway's trivia night raised nearly \$5,000 boosted by his employer NAB matching it with another \$5,000.

'Throw the Book at MS' raised another \$6,000 and organiser Jo Dwyer said 'We provide questions on books-and-writers theme, and next year we want all book groups to play the game and pass around the hat at their June 2008 meeting – simple!' Book clubs can get on the list now by emailing johanna@dwyers.optusbiz.com

Merchandise sales from MS Awareness Week topped this up. Many thanks to everyone who helped make big and small fundraisers a success,' said Ian. 'Our ultimate goal is \$5m invested in Australian-based research for a cure for MS – so be part of the solution.'

Research funded by F5m

- \$75,000 from the Darebin Council function in late 2005 to Monash University to help Prof Claude Bernard and his Stem Cell research into MS
- \$152,000 has been allocated from Lina Marrocco in Melbourne, from Tattersall's (\$15,000) and from the masked Ball late in 2006 (\$137,000) – with \$68,000 being applied to our new MS Gene Mapping and Gene Expression research at Howard Florey Institute and the other \$84,000 being allocated to further neurobiological studies of MS at Howard Florey
- \$230,000 raised from the Trish Foundation in 2005 and 2006 has been applied – \$30,000 to an MS Scholarship, \$100,000 to the MS Brain Bank and \$100,000 to our major Gene Mapping research.
- \$42,000 raised in Adelaide earlier this year will be applied to a Proteomics research Platform, to be established in the University of Adelaide.

That's \$499,000 (let's say \$500k) or half the total – while the other half is in the bank ready to be allocated when required.

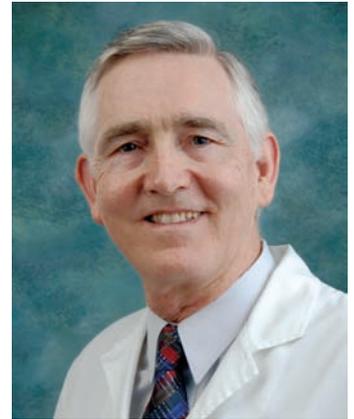
Some of the events already planned as we head to \$2m!

- Oct 12 Canapes and Canvas Spring Lunch in Brisbane organised by Natalie Walsh
- Oct 19 Concert at Turkish Embassy Canberra organised by Mary Webb
- Oct 20 Mystic MS dinner in Yeppoon, Qld organised by Karen Burkhardt
- Oct 28 Opera Harbour Cruise in Sydney, featuring soprano Toni Powell who has MS

To find out about these events or create your own fundraiser & be part of the answer to MS: log onto www.F5m.org.au or call F5m on 1300 356 467



Epstein-Barr virus under the microscope



Exciting research results from The Neuroimmunology Research Centre in Brisbane at the University of Queensland have led MSRA to commit a further \$500,000 over 2007-2009. 'The role of EBNA-1 in multiple sclerosis' project will continue to look at the relationship between MS and the Epstein-Barr virus (EBV).

EBV is the culprit for glandular fever and in the western world approximately 95% of adults are infected with the virus. It has the unique ability to infect, activate and persist without detection in important cells of the immune system.

MSRA previously invested \$110,000 in a **Research Fellowship to Dr Aleksandra Lenarczyk working with Professor Michael Pender and Associate Professor Scott Burrows** to investigate if people with MS have a defect in their ability to control the number of immune cells infected with EBV.

The first phase of research was based on a novel hypothesis from the Neuroimmunology Research Centre in Brisbane which continues its groundbreaking research investigating whether Epstein-Barr virus (EBV) infections trigger the development of MS in genetically susceptible people. The Centre's director, Professor Michael Pender, hypothesised that EBV infects large numbers of antibody-producing cells and that some of these cells stay in the person's brain – perhaps to play a role in determining when the immune system mounts an attack on the brain.

Preliminary results support the idea that MS patients tend to have a higher amount of EBV DNA in their blood. There's also evidence of a significant defect which affects the immune system of people with MS so that EBV goes unrecognised and persists in an increased number of infected immune cells.

Earlier research has suggested MS is due to an attack on the brain by white blood cells and antibodies – the cells of the immune system which defend the body against infectious diseases. No one knows why this immune attack on a person's own tissue is not switched off in people with MS but EBV is now being seen as a likely suspect.

If there is a causal link between EBV and MS, control of EBV-infected immune cells should inhibit the progression of the disease. This might be achieved through vaccination against EBV or through antiviral agents.

MSRA Partners

MSRA Multiple Sclerosis Research Australia

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