MS WIRE
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SCIENTISTS TAKE MAJOR STEP TOWARD CHANGING THE COURSE OF MULTIPLE SCLEROSIS

Australian researchers can study more than 100 genetic risk factors for multiple sclerosis (MS) together, a breakthrough that brings scientists closer to understanding how the disease develops and to improving quality of life for people living with MS.

The project, led by Dr Hamish King at WEHI and funded through MS Australia's latest $2.8m research grant round, addresses a long-standing gap in MS genetics.

Over the past two decades, large genetic studies have identified hundreds of small DNA changes linked to increased MS risk. However, most of these changes do not alter genes directly.

Instead, they affect how genes are switched on and off inside immune cells, making it difficult to understand exactly how they contribute to disease.

Until now, understanding how these genetic risk factors linked to MS act together to drive disease has been a major challenge for researchers.

Dr King's team will now introduce and test these genetic risk factors in human immune cells, measuring how they alter gene activity and immune behaviour both individually and in combination.

Dr King said understanding how networks of risk genes operate together could help enable more precise treatments and, ultimately, better long-term outcomes for people living with MS.

"For more than 20 years, we've known that there are many genetic markers linked to risk of developing MS, but we haven't been able to

CONTINUED ON PAGE 3

FROM THE CEO

ROHAN GREENLAND

I'm getting ready for this year's May50K, the single most important fundraising event that supports MS research in Australia.

Please, please, please join me, if you can, as a participant or sponsor.

Registrations are open now. Every step we take, every dollar we raise, will support life-changing MS research.

And you can have great confidence in the quality of the research that you fund. Last year, we commissioned the most significant review since the program commenced in 2004.

We did so to ensure that – after more than 20 years – our research program remained fit for purpose, strategically aligned, transparent and capable of meeting the evolving needs of people with MS.

The review panel – comprising people living with MS, leading researchers, senior neurologists and an international neuroscientist – has worked hard over the past 12 months, talking with the MS community and examining all aspects of what is an ambitious and sophisticated program.

And I am so pleased to report that the reviewers found that:

"... the MSA Research Program is a nationally significant and high-performing portfolio, delivering substantial scientific outputs, national infrastructure, consumer-relevant insights, and strong global engagement. Across domains, the program demonstrates solid alignment with the MS Australia Strategic Plan and with the needs and expectations of researchers, clinicians, people with MS, and international partners."

But the overall message is clear – the research funded by you – our wonderful fundraisers, donors and May50K participants – is making a massive difference to the lives of people living with MS not only here in Australia, but around the world.

This great, globally significant program and the world-class researchers it supports, would not exist without you and the May50K.

If you are able, please sign on and walk, run, roll, row or move however you can, for whatever distance you can, to raise much needed funds for MS research.

I am running for Claire, my cousin with primary progressive MS, and Jo, my niece's partner, who lives with relapsing remitting MS. These two amazing people inspire every step I take, as I push my increasingly arthritic body to run 150km in May, to be bookmarked by two half marathons, the first in Sydney and the second in Spitsbergen.

Join me, join the Australia-wide MS community, and take part in the May50K. It's fun. It's healthy. And it's for a damned good cause that will bring benefit to the 37,700 people living with MS across the country and the 3m people living with MS across the world.

If you can't participate and want someone to sponsor, scan the QR code to sponsor me. Every dollar gratefully received will spur me on to achieve my distance and fundraising goals. I will certainly be thinking of all my sponsors as I get into those tough last few kilometres of my two half marathons.

Rohan Greenland
CEO, MS Australia

CONTINUED FROM PAGE 1

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fully explain how they alter immune cell behaviour," Dr King said.

"MS can arise from many small genetic differences acting together, and this platform will allow us to study those changes collectively and connect them to the specific genes and pathways they affect."

MS is an immune-mediated condition in which the body mistakenly attacks the brain and spinal cord, damaging myelin, the protective coating around nerve fibres.

The disease can affect mobility, vision, cognition and energy levels.

In 2025, more than 37,700 Australians are living with MS, a 77.4 per cent increase since 2010. The total economic burden of the disease reached $3b in 2024.

As the number of Australians living with MS continues to rise, accelerating research across the full spectrum of the disease is increasingly urgent.

MS Australia's Head of Research, Dr Tennille Luker, said projects like Dr King's are helping researchers close a critical gap between genetic discovery and real-world impact.

"Identifying risk was only the beginning. Understanding how those genetic changes actually drive disease is what allows us to change its trajectory."

"Alongside this work, we are investing in research that slows progression, manages symptoms and improves quality of life. These projects strengthen our response to MS today while laying the scientific foundation for prevention and cures," Dr Luker said.

DR HAMISH KING, WEHI

In addition to MS Australia's core funding, the generous support of the Browne Family has funded a Postdoctoral Fellowship, awarded this year to Dr James Hilton at the University of Melbourne to develop new compounds to protect nerve cells in progressive MS.

Over more than two decades, MS Australia has invested more than $60m in MS research.

CEO Rohan Greenland said sustained national investment in research is essential to delivering real progress for people living with MS.

"Research is hope, and it reminds people living with MS that progress is possible, and that better treatments and prevention are within reach."

"None of this would be possible without the passion and commitment of our state and territory Member Organisations, our donors and the broader MS community. Together, we are accelerating the discoveries that will bring us closer to a world without MS," Mr Greenland said.

The research grants were formally launched at Parliament House in Canberra on 4 March at MS Australia's Advancing MS Research in Australia event, with speakers including Dr Monique Ryan MP and Ms Renee Coffey MP, highlighting the importance of sustained national commitment to MS research.

2026-27 PRE-BUDGET SUBMISSION

Art by Circular Blooms (@circularblooms on Instagram), an art project by Deanna, a person living with MS and a member of MS Australia's LEEP. Deanna creates digital art using MRI scans to challenge misconceptions about MS.

MS Australia's 2026-27 Pre-Budget submission highlights key funding priorities to improve the lives of Australians living with MS. MS Australia advocates for strategic investments in research, healthcare, disability, and aged care to address the growing personal and economic impact of MS.

Our submission has four asks that will improve the lives of people living with MS and reduce the economic impact of MS on the Australian health, disability, social services and aged care systems, including:

1. More funding for MS research and data:

There is a critical gap in funding for research to prevent people from developing MS and shorten diagnosis time.

- **$8 million** over five years for a National MS Biobank.
- **$300 million** over ten years for a Neurological and Neuromuscular Health Research Mission.
- **$1.3 million** over two years for the AIHW to undertake neurological data improvement activities.

2. Improved access to MS Nurses:

The number of MS nurses is declining and one-third of Australians living with MS do not have access to life-changing MS nurse care and have consistently worse health outcomes.

- **$6.5 million** to employ an additional 65 MS Nurses to improve access.
- **$1 million** to develop an MS Nurses National Strategy to expand the MS nursing workforce.
- **$3 million** over four years to fund an MS Nurses pilot project.
- **$120,000** over five years to develop an MS Nursing microcredential.
- **$90,000** over three years to provide scholarships for nurses undertaking the microcredential.

3. Better supports for people with MS living with Disability:

- People with MS living with disability need improved access to support from the NDIS.
- Fund a flexible, participant-focused NDIS with sustainable pricing for participants.
- Recruit, train, upskill and maintain a sufficient NDIA workforce.
- Attract, train, upskill and maintain a high-quality disability workforce.
- Improve housing and living supports.
- Develop a single, nationally consistent assistive technology program.
- Increase the rates of the Disability Support Pension, New Start Allowance and JobSeeker Payments.
- Support for the development of a new set of Australian poverty measures, including capturing the additional costs of living with disability.
- Implement the recommendations of the Disability Royal Commission.

4. Increased funding for people living with MS in Aged Care:

Older people living with MS are overlooked in the Aged Care system which negatively affects their wellbeing and quality of life.

- Increase funding to meet the needs of the over 220,000 older Australians waiting for Support at Home packages and assessments.
- Funding to ensure equity of services and funding for older people with disabilities.
- Implement the recommendations of the Inspector General's review of My Aged Care.

SAVE THE DATE

MELBOURNE 25.11.2026

NATIONAL SYMPOSIUM ON MS MEDICATIONS

30 YEARS AND BEYOND

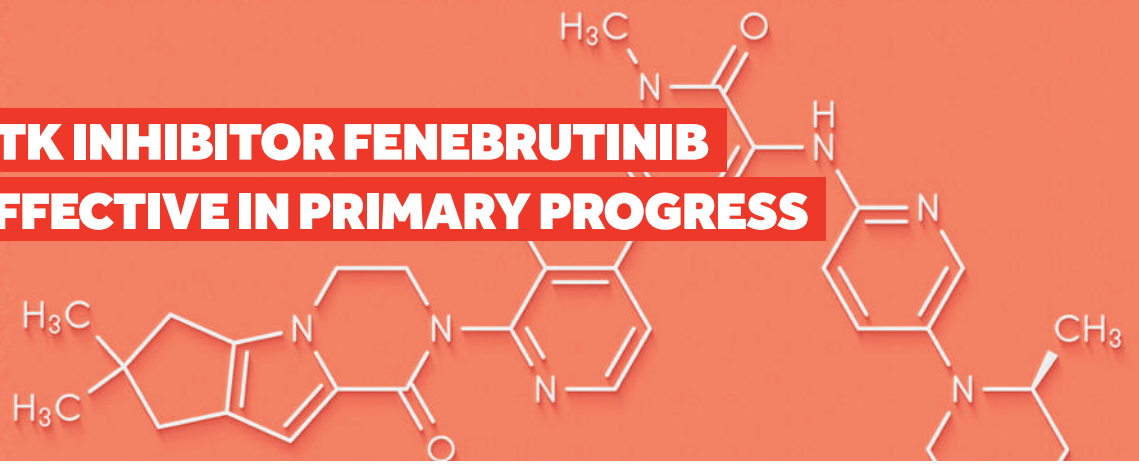
MS AUSTRALIA RESEARCH ADVOCACY CURE

The Florey Advancing Brain Research

MS AUSTRALIA RESEARCH ADVOCACY CURE

Find out more about MS Australia's research and advocacy initiatives

BTK INHIBITOR FENEBRUTINIB EFFECTIVE IN PRIMARY PROGRESS



What is fenebrutinib?

Fenebrutinib is an experimental oral drug being studied for its ability to treat both relapsing MS and primary progressive MS. It is in a class of medications known as Bruton's tyrosine kinase (BTK) inhibitors. BTK is an enzyme (a biological molecule that speeds up reactions within cells) that is important for many immune "B cells" as well as immune cells in the brain and spinal cord, known as microglia.

Because BTK inhibitors only target B cells that contain BTK, rather than all B cells, they offer a potentially safer and more targeted treatment than those currently available.

Fenebrutinib and primary progressive MS – the FENtrepid trial

There is currently only one medication, ocrelizumab, approved in Australia for primary progressive MS (PPMS), however, it is not listed on the Pharmaceutical Benefits Scheme (PBS). BTK inhibitors, which can penetrate the brain and spinal cord, therefore represent a promising treatment for progressive forms of MS.

A Phase III clinical trial of fenebrutinib in PPMS, FENtrepid, compared outcomes of participants on fenebrutinib with those on ocrelizumab.

The preliminary results, released in November 2025, showed that fenebrutinib was non-inferior to ocrelizumab as measured by the delay in the onset of composite confirmed disability progression over a period of at least 120 weeks of treatment.

New results from FENtrepid released

Compared with ocrelizumab, fenebrutinib was associated with a 12% reduction in the risk of disability progression. Although the trial was not designed to be able to determine this definitively, fenebrutinib appears to be a little better at limiting progression of disability in PPMS than ocrelizumab.

Results for the various components of disability progression were also analysed. The strongest treatment effect was seen for arm function, with fenebrutinib reducing the risk of worsening arm function by 26% compared with ocrelizumab.

Safety profile of fenebrutinib in PPMS

In general, the safety profile of fenebrutinib was similar to that of ocrelizumab. There were common side effects in at least 10% of participants, including infections, nausea, and haemorrhage.

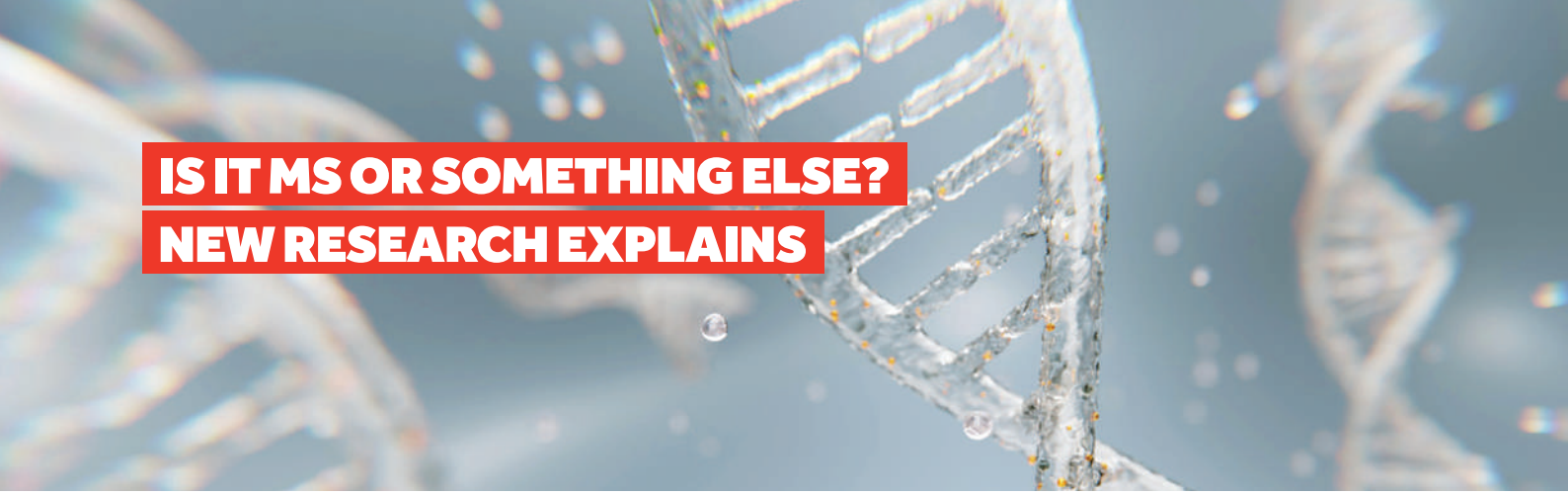
BTK inhibitors are known to raise liver enzymes in some individuals. In FENtrepid, increased liver enzymes were observed more frequently in participants receiving fenebrutinib than ocrelizumab (13.3% vs 2.9%). However, these were temporary, and all cases resolved when the study treatment was stopped.

There were no cases of severe liver injury in this study, a safety issue that has been seen occasionally in trials of other BTK inhibitors.

What does this mean for people with MS?

FENtrepid is the first positive Phase 3 clinical trial for PPMS in over a decade. The results suggest that fenebrutinib may represent a highly effective oral treatment for PPMS, directly targeting the biology of progressive disease in the brain.

Given that ocrelizumab is currently the only approved therapy for PPMS in Australia and is not PBS listed, the prospect of a second treatment option represents a significant milestone toward improving access to treatments for people living with PPMS.



IS IT MS OR SOMETHING ELSE? NEW RESEARCH EXPLAINS

Understanding MS mimics and genetic complexity

Many factors contribute to MS risk, including environmental and lifestyle factors and genetics. In fact, more than 200 genetic changes are linked to a slightly increased risk of MS, underscoring the complex interplay between genes and other risk factors.

Some rare neurological conditions, such as hereditary spastic paraplegia (HSP), CADASIL, Fabry disease, and certain leukodystrophies, can resemble MS or occur alongside it.

How often people diagnosed with MS actually have an alternate diagnosis (MS mimic) or genetic multimorbidity (multiple genetic conditions in the same individual) is unknown. It is also unclear whether rare genetic changes linked to other neurological disease genes play a role in who develops MS or how severe it becomes.

To address these questions, researchers from the Australia and New Zealand MS Genetics Consortium (ANZgene), a genetics research platform funded and coordinated by MS Australia, conducted a large-scale genetic study.

What did the researchers do?

The researchers collected genetic information from 4,340 people with MS seen in specialist MS clinics in Australia and New Zealand, along with 2,861 people without MS from the same regions.

They examined the protein-coding regions of DNA, focusing on 1,680 genes already known to cause other progressive brain and nerve diseases, to identify rare genetic changes that might affect brain and spinal cord function.

When potentially significant genetic changes were found, experienced MS neurologists reviewed those individuals' clinical histories and MRI scans in detail, without knowing the genetic findings initially, to determine whether they truly had MS, a different rare genetic disease, or both.

Finally, the team compared genetic patterns across large groups of people with and without MS, and among those with milder or more severe forms of MS, to see whether these rare genetic changes were more common in MS or associated with relapsing versus progressive disease and greater disability.

What did the researchers find?

Among the people with MS, 166 carried a genetic change significant enough to warrant closer clinical review, but detailed histories were only available for 75 of them. Of those 75, only four individuals showed clear evidence of either a genetic "mimic" disease instead of MS or a second genetic disease alongside MS.

When the researchers looked more broadly at all 1,680 genes linked to progressive neurological diseases, they did not find strong evidence that rare genetic changes in these genes were more frequent in MS than in people without MS, or that they were associated with greater MS severity.

What is the significance of this?

For people living with MS, these results are reassuring – in a large, well-characterised group seen in specialist MS clinics, misdiagnosis due to a genetic mimic or the presence of an additional rare genetic disease was very uncommon.

This study suggests that rare genetic changes in genes linked with other neurological diseases make little overall contribution to who develops MS or how severe the disease becomes.

MEET THE RESEARCHER

ASSOCIATE PROFESSOR ANNA HATTON

THE UNIVERSITY OF QUEENSLAND

TELL US ABOUT YOUR RESEARCH PROJECT

Our current project is testing whether sensory shoe insoles can improve balance and mobility. Participants wear the insoles for four weeks, during which we assess their performance in balance tasks that mimic real-world situations where falls are likely, and record how their leg muscles and nerves respond. We also interview participants to learn from their experiences using the insoles. The goal is to determine whether sensory insole technology can meaningfully improve balance and guide a future trial aimed at reducing falls.

WHY IS THIS RESEARCH IMPORTANT AND HOW WILL IT INFLUENCE THE UNDERSTANDING AND TREATMENT OF MS?

Many people with multiple sclerosis – about three in four – lose some feeling in their feet. This sensory loss is a major cause of poor balance and falls. Most treatments for balance problems, such as exercise programs, have limited effect because they do not target this underlying sensory loss.

Our research is testing innovative 'Vibrotexture' shoe insoles that boost the signals the feet send to the brain, helping the body react faster and stay steady. Using advanced balance we can see exactly how the insoles affect movement. The goal is to develop a clinically ready insole that can be used worldwide, making everyday life safer for people with multiple sclerosis and shaping future treatments that focus on foot sensation.

WHAT DO YOU THINK HAS BEEN THE MOST EXCITING DEVELOPMENT IN MS RESEARCH?

Within my field, one of the most exciting developments in multiple sclerosis research has been the growing focus on symptoms that have traditionally been overlooked – particularly altered foot sensation. Over the past decade, research teams around the world, including our own, have been pioneering and testing new medical technologies that target foot sensation, and this area is gaining increasing attention.

HELP FAST TRACK A CURE FOR MS

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To support MS Australia's vital work I would like to:

- ☐ Make a one-off donation of $
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PAYMENT METHOD

- ☐ **Cheque** $ made payable to MS Plus Ltd
- ☐ **Direct Debit Request** $ *copy of service agreement can be provided on request*

Financial institution

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Account holder's name

CREDIT CARD ☐ Mastercard ☐ Visa ☐ Amex

Credit card no.

Expiry date CVV

Name on card

Signature

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