# MND Research Network Newsletter Autumn 2022

Welcome back to our first newsletter of 2022. I hope you had time to relax and unwind over the summer months. As we start 2022 adjusting to life with COVID-19 in our community we hope its impact on the progression of research studies will lessen over the months ahead.

For those of you working in our hospitals and health care services it has also been a challenging time working on the front line under different pressures, and reprioritising workload. The months ahead will be difficult for some as case numbers remain high and we can only hope for brighter days ahead as we push through this phase of the virus.

In this edition you can read about the upcoming Australian and New Zealand MND symposium. Initially due to take place in November 2021 and then March 2022 it has now been confirmed for 28-30 April 2022. Registration is open, with a virtual option for those unable to travel.

We also provide an update on national research news including two new research projects starting this year. Dr Alan Stanley and a team of researchers are conducting a study to explore the economic costs associated with the care of people with MND living in New Zealand. The second study offers an exciting opportunity for someone who is interested in pursuing a master's qualification fully funded by MND NZ. This research will investigate the prevalence of MND in New Zealand — an important question that may help guide future MND research in Aotearoa.

The Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital (MGH) in partnership with ALS Finding a Cure® (ALSFAC) and FightMND is issuing a request for applications for the ALS Scholars in Therapeutics Program. This is an exciting opportunity for clinician-scientists and post-doctoral fellows to gain training and experience in therapy development for MND/ALS at their home institution.

If you have a question about MND research or you would like us to feature a specific topic, please email the network. If you know anyone interested in MND research, please encourage them to connect with us via Twitter, Facebook, or the MND Research Network website.

Kia kaha

Dympna Mulroy
NZ MND Research Network Manager

## Australian and New Zealand MND Symposium


The 2022 Australia and New Zealand MND Research Symposium will take place in Brisbane on Thursday 28th and Friday 29th April 2022 with an MND Connect - Research Live session on Saturday 30th April. Registration is now open with a **virtual option** for those who cannot travel to Brisbane. Hosted by FightMND and MND Research Australia, this is the first joint symposium between New Zealand and Australia. If successful it is hoped this partnership will continue to be a longer-term arrangement alternating between countries to host.

Please keep an eye on the symposium website for details on the programme announcement. We will also send updates via Facebook and Twitter.

## Research Opportunities

### Prevalence of MND in New Zealand – Masters Student Scholarship

An exciting research opportunity has become available for those interested in completing a master's degree and contributing towards the New Zealand MND research portfolio.

MND New Zealand is funding a study on the *''Prevalence of MND in New Zealand ''*. This is a nationwide, point prevalence study of MND in New Zealand using capture-recapture methodology. It is anticipated that this project will take place over 12 months. They are offering a $10,000 stipend (tax free), plus domestic tuition fees for 1 year. Enrolment is closing soon! This is an exciting opportunity to kick start a research career and make a significant contribution to the rapidly evolving field of MND research. More information is available on The University of Auckland Find a Thesis website or click here for details. Please share this with others in your network who may be interested.

### ALS Scholars in Therapeutics

Applications are now open for the ALS Scholars in Therapeutics Program. This two-year program is designed to engage clinician-scientists and post-doctoral fellows to gain training and experience in therapy development for MND/ALS at their home institution with an optional industry experience in year two.

### Award Details

2 years of funding to support a clinician-scientist or post-doctoral fellow working in the MND/ALS field anywhere in the world. $150,000 USD award/funding year (inclusive of maximum 15% indirect costs).

### Eligibility

- Applications from clinician scientists and postdoctoral fellows focused on translational research are eligible.
- Candidates with Ph.D. or M.D. with a strong publication record. International applicants are encouraged to apply.
- The MND/ALS focused proposal must have a strong scientific rationale and should be largely developed by the candidate with guidance from his/her mentor.
- Eligibility for this award is based on the date the candidate attained their degree/ qualification. For MDs, scholars will be considered if they have completed their specialist qualification (i.e., US Residency; Fellowship of the Royal Australasian College of Physicians, etc.) For PhDs they can be no more than 5 years post- degree.

Click here for further information **Applications close: April 29, 2022**

## MND Research New Zealand

### Costs Associated with Motor Neurone Disease in Aotearoa New Zealand

Dr Alan Stanley neurologist at Hawkes Bay DHB, is leading a study with a team of researchers that aims to estimate from a societal perspective (government and individual) the 1-year direct health care and indirect productivity loss, including informal care cost, of MND per capita in Aotearoa New Zealand in 2021.

Currently there is no information available about the health and social services people diagnosed with MND are using and the cost of these to government and to the person with MND and their whānau/family. The purpose of this study is to understand MND health care and support costs, and whether any funding gaps exist in health care and social support for people with MND. This information will assist MND New Zealand in advocating for the needs of people living with MND in New Zealand.

## MND Registry

The New Zealand Motor Neurone Disease Registry was established in 2017. Since its inception 362 people have enrolled. The MND Registry collects demographic, contact and clinical information, as well as genetic information if this is known. It uses the ALSFRS-R disability scale as a data gathering tool. This data can help to identify participants for clinical trials, help in the development of care standards, support specific research questions, increase knowledge about the disease, and connect patients and the research community. The Registry has facilitated entry of participants into thirteen studies including an upcoming clinical trial for symptomatic people with *C9orf72* genetic mutation.

As well as enrolling people with MND, the MND Registry will also enrol people without MND who have a family member with an identified genetic form of MND. Individuals can register online or email to request more information.

If you are gathering data on MND to assist with a research question or you would like to recruit participants with MND to an upcoming study, you can contact mndregistry@adhb.govt.nz for more information.

## Publications

Below are recent publications from New Zealand MND researchers

- Hippocampal protein aggregation signatures fully distinguish pathogenic and wildtype *UBQLN2* in amyotrophic lateral sclerosis - Thumbadoo, K. M., Dieriks, B. V., Murray, H. C., Swanson, M. E., Yoo, J. H., Mehrabi, N. F., ... & Scotter, E. L. (2022). (Pre-print before peer review)
- Novel and known transcriptional targets of ALS/FTD protein TDP-43: Meta-analysis and interactive graphical databases- Cao, M.C., Scotter, E.L. (2022). (Pre-print before peer review)
- TDP-43 pathology: from noxious assembly to therapeutic removal. Keating, S. S., San Gil, R., Swanson, M. E., Scotter, E. L., & Walker, A. K. (2022).

# MND clinical trials

The 32nd International Symposium on MND took place virtually last December. The MND Association created a series of blogs on the various presentations which included updates on clinical trials. You can read their two part blogs (part 1 and part 2) to learn more about the current clinical trials happening for potential new drugs for MND. All abstracts from the symposium are available to view here.

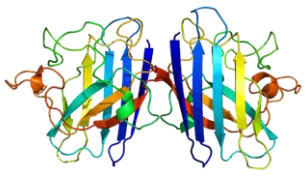
## Biomarkers in MND

One of the themes in the 32nd symposium was the use of biomarkers and incorporating them in early phase clinical trials to speed up the process. MND is heterogeneous in nature making it difficult to plan clinical trials and demonstrate similar benefits for this population group. Biomarkers can help to fill this gap. Grouping individuals with similar characteristics and monitoring levels of specific biomarkers during a trial can help establish if the drug or intervention being tested is influencing disease progression.

Associate Professor Mary-Louise Rogers from the Motor Neuron Disease Research program at the Flinders Health and Medical Research Institute recently wrote on an article on the importance of finding biomarkers in MND. She outlined the different types of biomarkers that can be used in clinical trials for MND treatments. Click here to read the full article.

## Tofersen (BIIB067) Biogen; Symptomatic Adults with SOD1-ALS

In past newsletters, we have been tracking Biogen's study of Tofersen for adults with SOD1-MND. SOD1-ALS is a rare, genetic form of ALS that accounts for approximately two per cent of the estimated 168,000 people who have the disease globally. Tofersen is an antisense oligonucleotide currently being evaluated for its efficacy in these patients. In the Phase 3 VALOR study, the primary endpoint as measured by the Revised Amyotrophic Lateral Sclerosis



Functional Rating Scale (ALSFRS-R) did not reach statistical significance; however, signs of reduced disease progression across multiple secondary and exploratory endpoints were observed. Considering the critical unmet need, Biogen has expanded eligibility for its early access program (EAP) to all eligible people with SOD1-MND to access tofersen outside of a clinical program and commercial setting.

What you need to know:

- Tofersen is an investigational drug currently being studied in clinical trials. It has not yet been approved for commercial use for treating SOD1-MND by Medsafe and its safety and efficacy have not been established.
- The EAP is open to all people with symptomatic MND who harbour a *SOD1* gene mutation and are not involved in any other clinical trial or access program.
- Treating healthcare professionals can submit requests on behalf of patients who meet the above criteria by emailing MedicineAccess@clinigengroup.com - Biogen cannot accept requests directly from patients. The full details can be requested when making an enquiry via the above email address.
- Biogen Early Access and the Guiding Principles can be located here.

This major milestone in MND treatment development emphasises the importance of genetic testing in MND. This has been highlighted in recent years in New Zealand with a current national study examining the genetic causes of MND, led by Dr Emma Scotter and Dr Richard Roxburgh at the University of Auckland. This is a national study of which any patient with MND (or a family member where genetic MND has been demonstrated or where there is a pattern of familial MND) can take part in.

The research team have submitted the following abstract to the upcoming Australian and New Zealand MND symposium, which summarises study findings (omitting controls) to date:

## Genetics of Motor Neuron Disease in New Zealand

Miran Mrkela[1], Miriam Rodrigues[2], Jules Devaux[1], Siobhan Kirk[1], Chitra Vinnakota[1], Christina Buchanan[2], Dympna Mulroy[2], Harry Fraser[2], Hannah Reid[3], Kylie Drake[3], Elsa Parker[3], Howard Potter[3], Emily McCann[4], Lyndal Henden[4], Kelly Williams[4], Jasmine Connell[5], Sam Eiszele[5], Anjali Henders[5], Naomi Wray[5], Richard Roxburgh[1, 2], Emma Scotter[1]

1. University of Auckland, Auckland, NZ
2. Auckland City Hospital, Auckland, NZ
3. Canterbury Health Laboratories, Christchurch, NZ
4. Macquarie University, Sydney, Australia
5. University of Queensland, Brisbane, Australia

*Incidence and mortality of motor neuron disease (MND) in New Zealand are among the highest in the world. Because MND risk is determined by both genetic and environmental factors, we sought to understand the high rate of MND in New Zealanders by characterising its genetic aetiology.*

*Participants had sporadic or familial MND, or were relatives of familial MND cases. DNA was tested by C9ORF72 repeat-primed PCR; Sanger sequencing (SOD1, TARDBP, FUS, and UNC13A); and genome-wide screening array for MND-associated variation in 17 other genes, and identity-by-descent (IBD) analysis. Familial or young-onset (<35 y) MND cases, or those related (IBD) to another MND case, were also sequenced (next generation) for a commercial panel of 42 genes (Invitae). Pathogenic variants were validated clinically and reported back to participants with MND.*

*We identified pathogenic variants in 16 of 103 participants (16%); 2 of 79 sporadic (2.5%), 4 of 9 familial (44%), and 10 of 15 unaffected relatives (67%). These were C9ORF72 repeat expansions and SOD1 p.Glu101Gly and p.Ile114Thr variants. A SOD1 p.Ile114Thr-positive individual was related to a cluster of >50 individuals from Australia and the UK with the same variant. Ten participants with sporadic MND (13%) had variants of unknown significance; 3 with the NEK1 p.Arg261His variant. The UNC13A rs12608932 C/C variant was seen in 6 sporadics (7.6%) and 1 unaffected gene-positive (10%) participant.*

*The genetics of MND in New Zealand resemble those of Australia and the UK. Unaffected relatives of familial cases harboured the majority of the identified pathogenic variants, representing an urgent need for pre-symptomatic interventions.*

You can hear more about this study at the upcoming MND symposium in April.

As our borders reopen and restrictions lessen, we welcome more opportunities that enable us to network again in person, starting with the Australian and New Zealand MND symposium. We hope to see you there in person or virtually.

*"Research is formalized curiosity. It is poking and prying with a purpose."* (Zora Neale Hurston)