

FIGHT MND.

Researcher.

PROF JULIE ATKIN

IMPACT Project.

**DISEASE
SUSCEPTIBILITY,
PRECISION MEDICINE
AND ALS**



Prof Julie Atkin

Where do you work?

At the Macquarie University Centre for Motor Neuron Disease Research, a recognised centre of expertise within the university.

What is your research experience and background?

I am a cell biologist/biochemist and I have worked exclusively on MND for the last 16 years. My research involves investigating the basic cellular processes that trigger neurodegeneration in motor neuron cells in this disease.

Which of your scientific findings so far do you value most?

We were the first group to identify the normal function of C9orf72, the protein which becomes mutated in the most common genetic forms of MND. We have also uncovered several molecular pathways that are triggered in MND. From this, using funding obtained previously from FightMND, we are developing drug-like compounds as possible new treatments. These compounds are based on accurate understanding of the underlying cellular mechanisms involved in MND.

Can you describe the current focus of your research team?

My group aims to discover at the molecular and cellular level what makes motor neurons begin to degenerate and ultimately die in MND, with the aim of designing new drugs to prevent this from happening.

What is exciting to you about the Macquarie Neurodegenerative diseases biobank?

The scale and scope of the patient samples available in the Macquarie Neurodegenerative Diseases Biobank is unique in Australia. The Macquarie Neurology clinic, led by Professor Dominic Rowe, treats approx. 10% of Australians living with MND (~220 patients), and we collect blood, urine, hair and skin biopsies from participants at each visit. Importantly, we have extensive clinical information available, and we can assess patients as the disease progresses over time, providing valuable insights into the disease mechanisms involved in MND. We also have the unique opportunity to integrate our findings with other studies using the biobank in the Centre. Our biobank is therefore unparalleled in its breadth of MND samples for which detailed clinical information is available. In addition, we have been awarded NSW Health certification for the Biobank, which attests to the high-quality of our sample collection protocols and procedures for sample processing, which will ultimately improve the accuracy of our research findings. In summary we have access to a unique platform in Australia in the Biobank with an unrivalled set of clinical information.

What will this funding allow your team to achieve?

MND is very variable in terms of clinical symptoms, site/age of onset, disease duration, and its association with other conditions such as dementia. In fact, it is sometimes thought that MND is a

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group of disorders rather than a single disease. Remarkably, not all motor neurons in the body are targeted equally, which leads to this clinical diversity. This project aims to identify protein markers that dictate why specific motor neurons are more vulnerable than others in MND, leading to this clinical heterogeneity. From this, we aim to identify subgroups of patients that display unique

characteristics, in which specific therapeutic approaches may be more effective than in other types of MND. The protein markers we will examine have never been examined before with such an extensive collection of clinical samples. We therefore aim to lay the groundwork for the development of a 'precision medicine' approach to MND, to develop optimal targeting and timing of treatments.

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This project will make use of the extensive collection of samples from MND/ALS patients in the Macquarie University Neurodegenerative Diseases Biobank. This Biobank is unparalleled in Australia in its breadth of MND samples, for which extensive clinical information is available. It collects blood, urine, hair and skin biopsies from participants at each clinic visit over the course of disease. The high-quality of the biological samples in this Biobank is recognised with certification by NSW Health in March 2019.

This project aims to identify protein markers that are closely linked to the vulnerability of motor neurons in MND/ALS. We aim to identify subgroups of patients that display specific or unique molecular characteristics using these markers, in which therapeutic approaches may be particularly effective, using innovative new statistical approaches such as machine learning. These markers have never been examined before with such an extensive collection of clinical samples. We therefore aim to lay the groundwork for the development of a 'precision medicine' approach to MND, to ultimately develop optimal targeting and timing of treatments for MND. This project should therefore lead to tailored interventions and the development of precision medicine approaches in the future.

OBJECTIVES:

- To accurately identify and categorise MND/ALS patients into groups defined by the presentation of distinct biochemical markers and disease features.

OUTCOMES:

- Identify biomarkers of MND/ALS based on disease mechanisms and symptoms, that categorise specific patient subgroups, and can be used to determine therapeutic approaches for patients that optimally target their disease causes.
- Provide the first steps towards the development of new therapeutic strategies that are tailored to specific sub-groups of MND/ALS patients that share distinct symptoms.



Processing samples at the Macquarie University Neurodegenerative Diseases Biobank.