FIGHT MND.

Researcher.

A/PROF LEZANNE OOI

IMPACT Project.

DEFINING AN ELECTRICAL SIGNATURE OF SPORADIC MND, AND DEVELOPING A DRUG SCREENING TECHNOLOGY AND NOVEL THERAPY

Priority Area.

DISEASE BIOMARKERS AND MODELS

A/Prof Lezanne Ooi

Where do you work?

The Illawarra Health and Medical Research Institute and School of Chemistry and Molecular Bioscience, University of Wollongong.

Can you summarise your research experience and background?

I am an NHMRC Boosting Dementia Research Leadership Fellow and Group Leader of the Neurodevelopment and Neurodegeneration Laboratory. I am a cellular neuroscientist, and my research has spanned electrophysiology, molecular and cellular biology, and pharmacology.

What drew you to MND research?

I have researched in neuroscience for twenty years and in neurodegenerative disease research for fifteen years. One of the reasons I love working at the University of Wollongong is that I have some incredible colleagues and we work collaboratively on a number of projects. When I started my lab there in 2012, my colleagues inspired me to collaborate on an initial MND project and I developed my MND research program from there.

Can you describe the current focus of your research team?

My research team uses cells from patients, post-mortem tissue and other models of neurodegenerative diseases to investigate the molecular mechanisms underpinning diseases and to test potential therapeutic strategies.

Your project investigates a Motor Neuron's electrical signals. Can you tell us a little bit about what the electrical signals do?

Neurons communicate via electrical signals; the coordination of these electrical signals allow us to move, breathe, speak, and think. These electrical signals, and the way they are controlled (e.g., increased or decreased), underpins everything that we do in our daily lives.

How did you identify electrical signals used by Motor neurons are affected in MND?

It has been known for some time that patients with MND show alterations in the electrical signals of their motor neurons, and these changes can start even before the onset of symptoms. In our experiments, MND patients have donated skin cells and we use these to recreate their motor neurons in the laboratory. Importantly, the same changes in the electrical signals detected in living patients can also be seen in the recreated motor neurons. This means that patients' cells can be harnessed to investigate the disease process. We use electrodes to interrogate which specific signals are altered and how this affects the way the neurons communicate with one another.

FIGHT MND.

What will you be able to achieve with this funding?

We want to create a resource that can be used by researchers and that will have an impact for patients. This funding gives us the opportunity to couple our electrophysiology and cell biology data with computer science, in order to study the exact causes of those changes in electrical signals and test novel ways to prevent those changes. We thank FightMND and everyone who purchased Big Freeze 6 beanies for making this possible.

A/Prof Ooi and her team in the laboratory at the Illawarra Health and Medical Research Institute

The IMPACT Project

Motor neurons talk to each other using electrical signals. However, motor neurons are excessively active in MND, which prevents them from communicating appropriately. This constant excessive activity ultimately causes motor neurons to lose function and die, as demonstrated in preclinical MND models. Previously, this research team has shown that motor neurons developed from MND patient stem cells are also overactive. They are now predicting that the overactivity of these motor neurons can be measured to identify an electrical signature and biomarker of MND.

This project aims to identify how electrical signals change in motor neurons to make them unwell. The research team will use stem cells from MND patients to develop spinal cord-like motor neurons and 3-dimensional models of the cortex, called cortical organoids. Electrical signals used by motor neurons in these models will be assessed using cutting-edge technologies such as microelectrode array stimulation, machine learning and artificial intelligence. Investigators hope to identify an electrical biomarker signature of motor neurons affected by MND, and will attempt to modify their activity to enable them to function like healthy motor neurons.

OBJECTIVES

- Identify an electrical biomarker signature of MND.
- Develop a high-throughput drug screen platform using 3-dimensional 'organoid' models of MND, that measure a drugs ability to modify the electrical signalling of motor neurons.
- Develop protocols that modify electrical signalling and restore function to motor neurons affected by MND.

OUTCOMES

- A positive outcome for this project would be the development of a high-throughput screening platform for preclinical testing of new strategies aimed at reversing overactivity, loss of function and death of motor neurons.