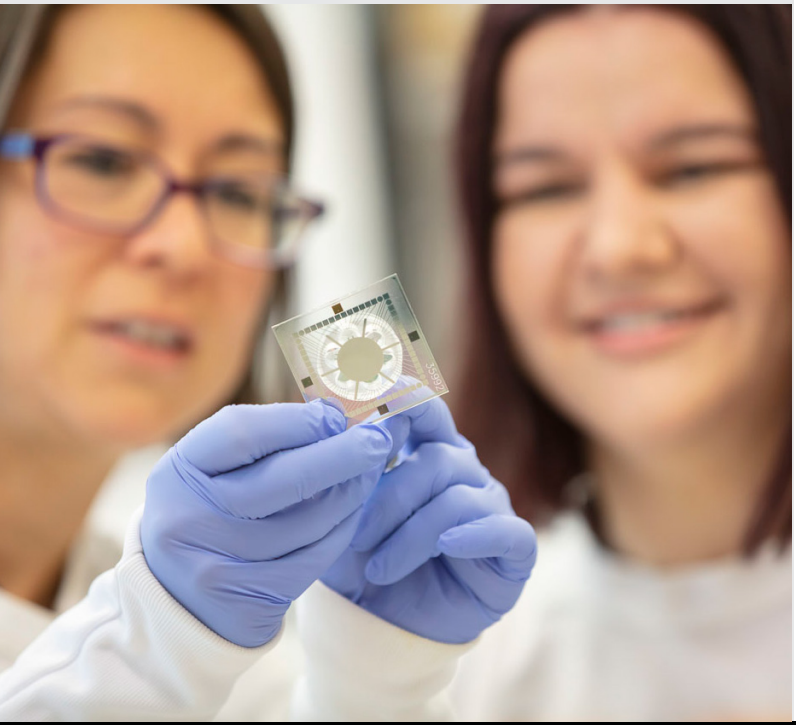
FIGHT MND.

Project

Gene therapies

Restoring autoregulation of TDP43 in MND using splice-switching antisense oligonucleotides

Investigators in this project are using a two-pronged genetic approach targeting a molecule called TDP-43, an important molecule in cells that has many functions. In almost all cases of MND, TDP-43 sticks together to form clumps that make motor neurons unwell. The first genetic drug being tested is designed to prevent the production of TDP-43 clumps in motor neurons. The second drug will restore levels of a molecule in motor neurons, which is essential for their health and repair, but whose levels are reduced when TDP-43 clumps form. The study will test the benefit of this combination genetic therapy in motor neurons made from MND-patient stem cells.



Project Lead

A/Prof Lezanne Ooi

University of Wollongong, NSW

A/Prof Lezanne Ooi's project uses stem cells that are 'reprogrammed' from skin cells donated by MND patients or healthy people. From these she and her team *"can make motor neurons that bear the same genetic sequence as patients."*

Motor neurons created from skin cells

A/Prof Ooi says she *"still finds it incredible that motor neurons created from the skin cells of MND patients show some of the same characteristics as can be measured in living patients. This provides an opportunity to use these cells to understand the traits of each person's disease and to test potential therapies."*

Bringing together experts from multiple fields

Currently working on TDP-43-targeted gene therapy, A/Prof Ooi explains how this therapy has potential for disease intervention.

"Several 'antisense oligomers' have been approved for use in the clinic in recent years, including for the treatment of spinal muscular atrophy, and Duchenne muscular dystrophy. This research brings together the strengths of experts in gene therapy, stem cells, inflammation and bioinformatics."

"It will be exciting to work with these talented collaborators," she says.

Funding from FightMND will help A/Prof Ooi and her team to *"test a combination gene therapy in cells from a range of patients to see if we can restore normal levels and function of TDP-43 and whether this strategy can protect motor neurons,"* says A/Prof Ooi.

"Toxic accumulation of TDP-43 protein into "aggregations" occurs in around 97% of MND patients, so if we are able to successfully restore TDP-43 to its healthy levels and functions, this has the potential to benefit many patients."

FightMND has invested $249,349 in this research

About A/Prof Lezanne Ooi

A/Prof Lezanne Ooi is a Principal Research Fellow and Group Leader of the Neurodevelopment and Neurodegeneration Lab at the University of Wollongong, Australia. She established her lab in the Illawarra Health and Medical Research Institute and the University of Wollongong in 2012.

A/Prof Ooi's research speciality is cellular neuroscience and the regulation of neuronal function in neurodegenerative disease. She trained in the UK and was awarded a Wellcome Trust Prize PhD with studies on gene regulation and neurodegenerative disease from the University of Leeds. During her post doctoral research, she studied the regulation of ion channels and signalling molecules and developed cellular imaging techniques and used electrophysiology to understand the control of neuronal excitability and function in development and disease.