FIGHT MND.

Project

Disease heterogeneity

Exploiting cryptic relatedness in global MND to uncover disease and phenotype-linked genes

MND affects people in a variety of ways. People living with MND experience different disease courses, with variable age of onset, progression and duration of disease. This study will perform a genetic analysis of 9,000 MND cases, aiming to uncover ancestral links between cases that may identify new genes that cause MND or influence disease progression.

"I am grateful to the everyday people who donate to FightMND to support research, even if they are not impacted directly by MND."

Project Lead

Dr Kelly Williams

Macquarie University, NSW

Dr Kelly Williams knew right from her undergraduate studies that she wanted to pursue a career in medical research, specifically in human genetics.

Offered a genetics Research Assistant position in Prof Ian Blair's MND group at ANZAC Research Institute in 2007, she was part of the team that discovered MND-linked mutations in TDP-43, only the second gene to be discovered to cause MND. This gene was discovered 15 years after the first and was an enormous breakthrough discovery in MND.

Dr Williams says *"knowing what a large impact this single gene discovery had made for people living with MND and their families, I was dedicated to continue working on MND genetics research until there are no more MND genes to be discovered."*

Genetics and genealogy

Dr Williams and her group are currently studying genetic research projects that analyse genome data of individuals with familial and/or sporadic MND. However, she notes that she does *"have a strong passion for working on the hereditary form of disease because it goes back to my classical genetics background - family trees, genealogy, haplotypes – it is what I enjoy doing most."*

"A gene discovery in an MND family may not be relevant to every person living with MND, but to those whom it may be relevant, it could change their family's future," she says.

Cryptic relatedness

Dr Williams explains *"cryptic relatedness"* as a situation where study participants are genetically related, but the relatedness is unknown to the researchers.

"MND cases who are related, even distantly, may share genetic factors that cause disease, increase disease risk, or modify the presentation of MND," she says.

"In traditional genetics studies, we separate hereditary and sporadic MND into separate groups for different analysis. However cryptic relatedness studies enable us to integrate all MND patients, bridging the gap between sporadic and hereditary MND to find shared ancestry from up to 250-300 years ago."

This IMPACT project, uncovers previously unknown relatives that have a shared ancestry and identifies the *"specific regions of the genome that they share"*. It will allow Dr Williams and her team to pinpoint the gene defects that contribute to MND.

"This will be directly beneficial to MND research as a large portion of what we currently understand about the biology of MND has come from gene discoveries," she said.

Relief, gratitude and excitement

Dr Williams said that when she first heard the news that she had received a grant her thoughts were *"firstly, relief and gratitude and then excitement."*

She explains that medical research funding is very competitive and that funds provided by FightMND ensure she can keep her team of early-career researchers together to continue their genomics research. She says she is excited that they now have two years to really focus on the project and deliver some impactful results.

A worldwide project

The IMPACT grant funding from FightMND will allow Dr William's group to take their cryptic relatedness study internationally to impact MND research around the globe.

"Not only will we be searching for cryptic relatedness in more than 3,000 Australian and New Zealand MND cases (many recruited through SALSA-SGC, funded by FightMND) but also more than 7,000 MND patients from Project MinE comprising Great Britain, Ireland, United States, Belgium, Spain, France, Israel, Italy, The Netherlands, Portugal, Sweden, Turkey and Switzerland," she says.

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FightMND has invested $250,000 in this research project.

About Dr Kelly Williams

Dr Kelly Williams works at the Centre for MND Research within the Faculty of Medicine, Health and Human Sciences at Macquarie University. She has been researching the genetic basis of MND for almost 15 years and has played a key role in most MND gene discoveries worldwide. Her early research background was classical genetics and molecular biology to uncover genes causing hereditary MND, and now includes bioinformatics and computational biology to align with the rapidly changing research field of human genetics and large-scale genomics. In 2013, she received her PhD in MND genetics, was awarded the Bill Gole MND Fellowship and was recruited to be a founding member of the Macquarie University Centre for MND Research.

Dr Williams established Australia's first ALS/MND gene discovery bioinformatics pipeline and led the setup of the largest Neurodegenerative Diseases patient sample Biobank in Australia. This is held onsite at Macquarie University and currently comprises in excess of 50,000 biological samples. Dr Williams was awarded an NMHRC Early Career Fellowship in 2016 for MND genomics and now leads the Genomics and Bioinformatics Group within the Macquarie University Centre for MND Research.