Researcher: A/Prof BRADLEY TURNER
Project: TARGETING THE METABOLISM OF GLYCOSPHINGOLIPIDS AS A NOVEL THERAPEUTIC STRATEGY FOR MND

Who are you and where do you work?
I am Head of the MND Laboratory at the Florey Institute of Neuroscience and Mental Health, University of Melbourne.

Can you give us a summary of your training/experience background?
I have been researching MND for over 15 years. I obtained my PhD in biochemistry at the University of Melbourne in 2005 and undertook postdoctoral training in functional genetics with Prof. Kay Davies and Prof. Kevin Talbot at Oxford University. I was recruited back to the Florey Institute in 2008 where I established the MND Laboratory.

Can you describe the work your lab is currently pursuing?
My group is pursuing a number of promising therapeutic clues for MND using novel gene and drug therapy approaches. We test our therapeutic agents in established patient-derived cell and animal models and fully embrace cutting-edge technologies and tools as they evolve. Our main focus at present is re-purposing prescribed medications for MND to expedite drug development.

How did you identify your compound(s) as a potential treatment for MND?
I have a longstanding collaboration with Prof. Michael Spedding based in Paris for drug re-purposing in MND. On one visit to Melbourne last year, Michael expressed excitement about one such compound over coffee and a few Skype meetings later, the collaboration was formed. We have assembled a team of international experts in MND and metabolism involving Dr Shyuan Ngo (University of Queensland) and Dr Alex Henriques and Prof. Jean Phillippe-Loeffler (University of Strasbourg) to accelerate preclinical development of our compound.

What excites you about this drug(s)?
This is a generic drug that is safe with a very good pharmacological profile and is ideally placed for rapid re-purposing and investigation in MND. This drug targets an underlying metabolic defect within motor neurons that corrects many key aspects of MND pathology. Early studies of our compound in animal models of MND are promising and we expect our compound will have therapeutic reach in sporadic MND.

What difference will the awarding of this grant make to your work?
This awarding of this grant will enormously accelerate pre-clinical development of our lead compound to leverage evidence and support for potential clinical studies.

This grant also catalyses a novel interstate and international collaboration between academia and industry for MND that would not be possible otherwise.

THE PROJECT
TARGETING THE METABOLISM OF GLYCOSPHINGOLIPIDS AS A NOVEL THERAPEUTIC STRATEGY FOR MND

MND is a complex and multifactorial disorder. There is increasing evidence that abnormal energy and lipid metabolism within nerve cells and muscles contributes to the disease course and underlying motor neuron pathology. We recently discovered a defect in a critical biochemical pathway responsible for producing specialised cell lipids called "glycosphingolipids" in MND which are essential for motor neuron function and connections in the nervous system. Excitingly, we have identified a lead drug that can correct metabolism of glycosphingolipids in mouse models of nerve injury and MND, slowing both disease progression and motor neuron pathology. Importantly, our lead compound is a safe prescription medication that we seek to re-purpose for MND for the first time.

In an effort to rapidly progress development of our lead drug for MND, we have established a novel international collaborative project across multiple research teams. We will firstly comprehensively and rigorously evaluate our lead drug in established and emerging animal models of MND that are more applicable to sporadic disease. This is important to ensure that glycosphingolipid metabolism is a wide and relevant target for MND.

We predict our lead drug will improve motor neuron survival, connections with muscle, motor function and lifespan across multiple animal models of MND. Secondly, we will screen drug libraries for more potent and active compounds with improved delivery to the brain to correct glycosphingolipid metabolism using MND patient-based Petri dish and animal models of MND. This will provide crucial support for the continued re-purposing of our lead compound and development of next-generation drugs correcting glycosphingolipid metabolism to improve motor neuron health and connections in MND.