

Researcher: PROF TRACEY DICKSON
Project: PRECLINICAL DEVELOPMENT OF NEUROPEPTIDE Y FOR THE TREATMENT OF MND

Who are you and where do you work?

My name is Tracey Dickson, I am an Associate Professor of Neuroscience and the Deputy Director at the Menzies Institute for Medical Research.



Can you give us a summary of your training/experience background?

My PhD studies were performed at the University of Tasmania, where I graduated in 2000. I was awarded an NHMRC Fellowship to undertake post-doctoral training at the Mount Sinai School of Medicine, in New York City, and then to return to Hobart in 2003 to begin to start my own research group.

How did you come to work in MND research?

I have always been interested in the brain and how it works. But equally I have always been motivated to use this knowledge to help people. As I began to work on MND, and to meet people with MND and their families and carers, hearing their stories and experiences inspired me to focus my research on this devastating disease. It felt like it was a field of research where I could make a difference.

Can you describe the work your lab is currently pursuing?

I have been dedicated to researching the mechanism of MND for the last 10-15 years. We are now poised to transition our research efforts from determining the cause of MND, to now using this knowledge to develop a cure. There is considerable evidence from many areas of clinical and laboratory medical research that in MND the motor neurons are dying due to a toxicity that is triggered due to their over-activity - known as excitotoxicity. We now have new evidence that this toxic cascade is initially triggered by the death or dysfunction of another type of neuron in the brain -the interneuron. Interneurons are critical regulators of motor neuron activity and modulators of the balance that is essential for normal brain function. Importantly we have discovered that not all interneurons are affected, and we have identified the two specific populations through which this dysfunction is driven. The goal of our work that will be funded by the Cure for MND Foundation is to determine if we can treat MND with a drug that mimics the action of one of these specific types of inhibitory cells - Neuropeptide Y. Awarding of this grant will allow us to perform this world first preclinical trial, and gather the evidence needed to progress this drug to the clinic.

What excites you about this drug?

Excitingly, this drug has already been approved to undergo clinical trials for other neurological conditions, which means that if we can prove that it is effective in our experimental models then the pathway to the clinic and to patients with MND will be much quicker, as much of the required early safety and efficacy trial work has already been undertaken. This is an ambitious program of work. However, I am confident that our research team has the necessary expertise and skills required to significantly contribute to MND therapeutic development. We can't wait to get started, and are incredibly thankful for this opportunity.

THE PROJECT

PRECLINICAL DEVELOPMENT OF NEUROPEPTIDE Y FOR THE TREATMENT OF MND

Motor Neuron Disease (MND) is a rapidly progressive neurodegenerative disease. There are no cures and no effective treatments for MND, with people diagnosed having a median survival of only three years from symptom onset. Not knowing the cause of MND or how it progresses through the central nervous system (CNS) have been immense barriers to the development of effective therapeutics.

Our team has been dedicated to researching the mechanisms of MND for the last ten years. We are now poised to transition our efforts from determining the cause of this disease to using this knowledge to develop new treatments. A pathway that our work and others have shown is key to MND is altered network excitability and subsequent excitotoxicity in the cortex. We have recently published and preliminary data which identifies that a potential point of intervention in this pathway is via the subclass of inhibitory neurons that express neuropeptide Y (NPY).

The overarching aim for this Translational Research Grant is to now target this pathway to develop a treatment. By performing this world-first pre-clinical trial, we will reveal further aspects of disease pathogenesis. Positive outcomes from these trials will identify a candidate compound for progression to a human trial for the treatment of MND.

In this 3-year project, our objectives are to:

1. Determine the optimal dose of Neuropeptide Y that rescues MND neuronal pathology in vitro
2. Perform a pre-clinical test testing Neuropeptide Y as a therapeutic for sporadic and familial MND
3. Test a non-invasive method for delivering Neuropeptide Y to the corticomotor system

If our hypothesis is proven correct, then we would expect to be able to initiate a Phase 1 clinical trial at the end of this three-year project. We have been dedicated to researching the mechanisms of MND for the last ten years. We are now poised to transition our research efforts from determining the cause of MND, to now using this knowledge to develop a cure.

