Overview

As the Scott Sullivan MND Research Fellow, I oversee a team of researchers who are conducting translational research across The University of Queensland (UQ) and The Royal Brisbane & Women’s Hospital (RBWH). The laboratory where my team conduct all of our benchwork is based in the Australian Institute for Bioengineering and Nanotechnology (AIBN) at the UQ St Lucia campus. Our clinical research is based at the RBWH, and the Centre for Clinical Research (UQ), which are both located at the Herston Campus.

My team’s clinical research focuses on generating a better understanding of how the body responds to MND, and why this might be different between patients. Working with patients, we study the relationship between energy supply and use, dietary intake, gut function, physical activity and disease progression. By studying multiple aspects of physiology, our goal is to understand MND on a patient-by-patient basis. Our clinical research is supported by a strong collaborative network. Locally, we work closely with A/Prof Robert Henderson and Prof Pamela McCombe at the Royal Brisbane & Women’s Hospital and Wesley Hospital. To broaden the international reach and impact of our research, and to build capacity to establish an enduring framework that will support the translation of our research into future clinical trials, I have established collaborations with two internationally recognised and highly-regarded MND neurologists in the Netherlands (Prof Leonard van den Berg) and the United Kingdom (Prof Ammar Al-Chalabi).

My team’s laboratory-based research aims to identify the mechanisms that cause MND, and the molecular changes that occur as a consequence of MND, so that we can identify targets for drug development. Necessarily, our laboratory-based research is also highly collaborative, supporting my vision to deliver research findings that are clinically meaningful. We work with researchers across Australia, France, Italy, USA, and China who have expertise in drug development, physiology, biochemistry, genetics, statistics, and stem cells.

Research Update

Clinical research:

In 2018, we published the first results from our patient studies, showing that hypermetabolism (when energy use is higher than what is expected) occurs in MND patients who have faster functional decline and that hypermetabolic MND patients are at risk of earlier death. Paradoxically, this increase in metabolism was not related to weight loss, which is thought to be a major contributing factor to faster disease progression in MND.

To understand why changes in metabolism might be the occurring in MND, we have been studying diet diary information and the gut microbiome of each patient to understand if dietary intake and gut health might be linked to increased energy use in MND. We are in the final stages of analysing this data and our results suggest that there are significant differences between the dietary composition in MND patients when compared to non-MND individuals, but that the gut microbiome appears to be mostly unchanged. Collectively, these studies have now led to the development of a novel research program by our collaborator, Dr Frederik Steyn, who is investigating how changes in appetite and diet can impact weight loss and overall energy balance in MND. This collaborative research is
progressing well; we have recently published data to show that about 30% of MND patients have reduced in appetite, and that changes in appetite appear to be a primary factor for weight loss in MND.

In our clinical research, we are also tracking physical activity in our patients to see if the energy that they are expending is being offset by the amount and type of food that they are eating. A benefit to tracking physical activity in MND patients is that we are also able to ask important research questions about fatigue. We have found that about 70% of our MND patients experience severe fatigue, and we are now aiming to develop new ways to help MND patients manage their fatigue symptoms. Working with our Prof Leonard van den Berg’s group in the Netherlands, we are also aiming to determine whether the use of activity trackers can be used a means to remotely monitor disease progression in MND patients.

A dynamic young researcher, Ms Diana Lucia has recently joined my research team, and will be working closely with our MND patients in the coming year. She has a strong research background in circadian rhythms and will be further driving this area of research within the team. Diana also has a strong science communication portfolio. Since joining the team, she has volunteered at a number of MND and Me Foundation events, and will be continuing to do this in the future.

I would like to take this opportunity to thank all of the MND patients, their carers and family and friends, as well as all of the other volunteers who are involved in our research. The work that my team do in the clinic would not be possible without your contributions.

Laboratory-based research:

To develop a better understanding of what might be causing hypermetabolism in MND, we have been collecting blood, and muscle and skin biopsies from our MND patients and control volunteers. We have been studying the blood to see if there are any molecules that might explain increased energy use in MND, and have found changes in the expression in a number of hormones that regulate energy supply and use in the body. In the coming year, we will be confirming this observation in a larger set of samples. We have an enthusiastic young scientist, Mr Cory Holdom, who is currently conducting his honours research project in this area of our research.

With our muscle biopsies, we are using the resident stem cells in the muscle to generate muscle fibres in a dish. We have been studying the way in which these muscle fibres use and generate energy and have found that muscle fibres from MND patients appear to use fat as a preferred fuel source. This is an interesting observation because muscle usually prefers to use sugar as fuel source to generate energy. We are now expanding on these results to understand why this change in fuel preference is occurring, and how this relates to the way that the body uses energy. Dr Siobhan Kirk, a postdoctoral research fellow in my
lab who has quickly mastered the skills in this area, is overseeing this part of the research with support from our research assistant, Ms Elyse Wimberger.

With the skin biopsies, we are turning skin cells into stem cells that we then turn into neurons. This work is being led by a truly exceptional PhD student in the group Mr Timothy Tracey, who is also working closely with Siobhan. More recently, Tim has mastered a new technique to turn skin cells directly into neurons, making us the first team in Australia to generate these directly reprogrammed neurons for studying MND. This new method is important because the resulting neurons maintain environmental signatures that can give us new clues into environmental triggers for motor neuron death. Similar to our muscle samples, we are using our neurons to study whether the way in which they use and generate energy is related to the changes in the way the body uses energy, and whether there are unique differences in neurons that have been generated from different MND patients. We hope that this information can help us to develop more targeted treatment approaches for each MND patient.

In the laboratory, we also using mouse models to test a number of drugs with the aim to improve function and survival. All of our mouse work is overseen by Dr Tesfaye Tefera, who has over 4 years experience in studying metabolism in mouse models of MND. Results from all of our mouse projects have been promising, and we are now testing these same compounds in the muscle fibres and neurons that we have generated from our MND patients.

In the last 6 months, my team have been training an undergraduate researcher, Mr Hao Wang, who will be commence his honours research project later this year. Hao’s project will be based across my laboratory and Dr Frederik Steyn’s laboratory, and aims to test a new compound that builds on historical work conducted in my laboratory, as well as recent observations that we have made in the clinic.

Overall, the young team of researchers in my laboratory have been working tirelessly to improve our understanding of MND, and to test whether the drugs we are repurposing are a promising treatment approach for MND. The majority of this work has been submitted for presentation at the 30th International ALS/MND Symposium in Perth in December 2019, and we are looking forward to getting feedback from our international peers.

I would like to thank the MND and Me Foundation and the RBWH Foundation for their generosity and continued support of my research. I would also like to thank the Queensland Brain Institute, and the Australian Institute for Bioengineering and Nanotechnology for supporting my research and members of my team. This has enabled me to progress my work, and to establish a strong group of dedicated early career researchers who are all working towards our ultimate goal of developing a drug therapy to combat Motor Neurone Disease.
Contact details

Dr Shyuan Ngo
Scott Sullivan Research Fellow
T +61 7 336 53847
E s.ngo@uq.edu.au
W uq.edu.au

CRICOS Provider Number 00025B