FIGHT MND.


Dr Mouna Haidar

Researcher.

DR MOUNA HAIDAR

IMPACT Project.

ESTABLISHING A NOVEL MOUSE MODEL OF SPORADIC MND

Where do you work?

In the MND Laboratory at The Florey Institute of Neuroscience and Mental Health, University of Melbourne.

What is your research experience and background?

I obtained my PhD in Neuroscience and am now a Postdoctoral Fellow in the MND Laboratory at The Florey headed by A/Prof Bradley Turner.

How did you begin your research into MND?

I have always had an interest in understanding how the brain works, both under healthy and diseased states. I am passionate in applying this knowledge to the MND field to help further elucidate what goes wrong in brain circuits and motor neurons in MND.

Can you describe the work you are currently pursuing?

I am using an innovative and powerful chemogenetic technique called “DREADD” technology, which allows for the selective and chronic activation of targeted neuronal populations in the mouse central nervous system. I am using this technique to experimentally model an early and common pathological feature which occurs in all MND patients, called brain cortical hyperexcitability, and the associated subsequent MND neuropathology and symptoms. Brain cortical hyperexcitability is a disease process occurring in MND in which motor neurons become electrically overstimulated and overloaded, leading to their demise.

Why did you choose to develop this model of MND?

Inherited MND is quite rare, occurring in only 10% of patients, with the remaining 90% of patients having sporadic MND. So far, translation of promising therapeutic outcomes from MND mouse models to patients have been unsuccessful. This is partly because most studies have utilised mouse models based on rare genetic forms of MND, which may not adequately replicate disease features common to the mostly sporadic MND population. Therefore, there is an urgent need to develop a preclinical mouse model relevant to sporadic MND patients.

What excites you about this model?

This is a world-first attempt to model features of sporadic MND in a mouse model. Our model opens an exciting and novel avenue to study the disease mechanisms of sporadic MND, and test therapeutic candidates in a mouse model which recapitulates the core features of sporadic MND.

What difference will this funding make to your work?

Funding for this IMPACT project from FightMND will allow for the development and validation of the first mouse model that displays core features of sporadic MND, which would have otherwise not been possible. This project will open up an exciting avenue to study the disease processes of sporadic MND and test therapeutic candidates in a novel and relevant preclinical model.

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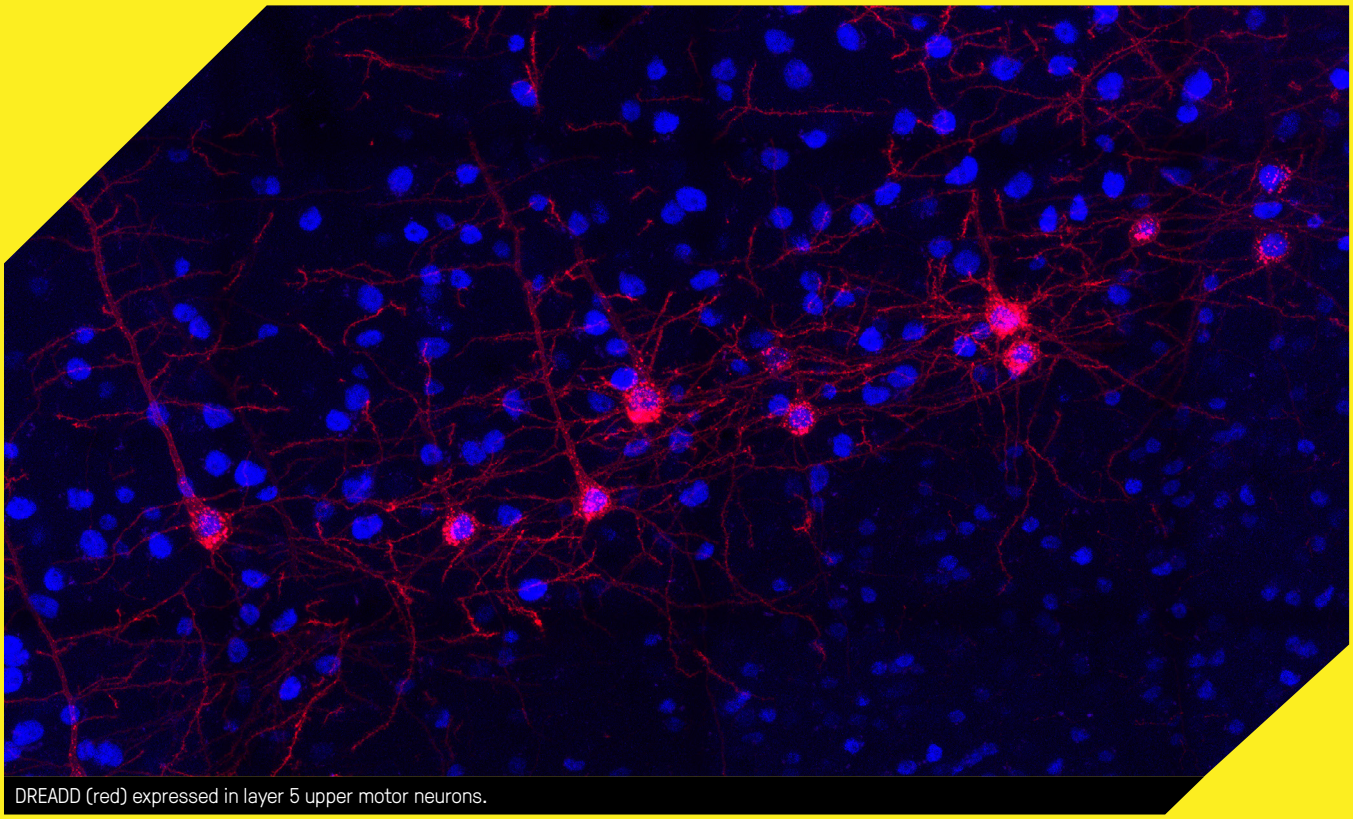
Inherited motor neuron disease (MND) occurs in only 10% of patients, with the remaining 90% of MND patients having sporadic disease. To date, translation of findings from MND mouse models to the clinic have been unsuccessful partly because most studies have been based on genetic mouse models of MND, which have subsequently failed in a mostly sporadic MND population. The failure to translate the positive outcomes of drug testing in mice into successful drug trials in humans has questioned the relevance of existing preclinical models for sporadic MND patients.

OBJECTIVE:

To overcome this major limitation, this project will develop a novel mouse model of sporadic MND that does not have genetic links. To achieve this, an innovative and powerful tool called DREADD technology will be used in mice to experimentally model the hyperexcitability and overactivity of motor neurons that occurs in all forms of MND.

OUTCOMES:

- Development of the first mouse model that mimics sporadic MND.
- Testing of potential therapeutic agents in this new preclinical mouse model aimed at preventing the onset/progression of MND.



DREADD (red) expressed in layer 5 upper motor neurons.