ANGIE CUNNINGHAM

PHD SCHOLARSHIP & GRANT-IN-AID

It is said that the qualities of a good PhD Student are perseverance, tenacity, courage, and the ability to communicate. The Angie Cunningham Cure for MND PhD scholarship and project grant-in-aid award honours the life and qualities of a woman who was the embodiment of all of these traits and more. Angie was a girl from Tassie who had not only a natural ability, but an undying perseverance. She applied this to her passion – tennis. At the age of 11, she conquered the national tournament and came to the attention of sports selectors. Her tenacity saw her leave home at the age of 14 to attend the Australian Institute of Sport, and she went on to hit a peak junior doubles ranking of No.2 and appeared in the Wimbledon girls' doubles final in 1991 as well as two Australian Open girls' doubles finals.

Later she went on to work as the vice president of player relations and on-site operations at the Women's Tennis Association. Her colleagues have said that it took 3 people to replace the work that she did for years on her own.

These qualities allowed Angie to stare down the barrel of MND with steadfast courage when she was diagnosed with the devastating disease at the age of 38. A wife to Pat, and a mother of 2 young girls aged 6 and 3, within days of the diagnosis Angie made a firm decision to "focus on the things that I have, not what I have lost".

Her ability to communicate and share her compassionate, loving spirit is something all of her friends can attest to. She was a mentor for young tennis players, a firm support for professional tennis players and colleagues, and a true friend. Her spoken word was full of humour and love, and it was these qualities that allowed her to navigate her journey with MND with dignity, grace and a complete appreciation for the value of life and love. She and Pat started the Laugh to Cure Campaign in 2014, before joining forces with Dr Ian Davis and Neale Daniher to form The Cure For MND Foundation.

Angie's legacy is that of courage, selflessness and eternal positivity against all the odds. To honour this legacy the Angie Cunningham PhD Scholarship and Grant-in-Aid has been established with the following objectives:

- to support research aimed at understanding the causes of sporadic MND, elucidating disease mechanisms and facilitating the translation of therapeutic strategies from the laboratory to the clinic.
- to encourage new interest within the field of Motor Neurone Disease research from exceptional new postgraduates.
- to help develop PhD graduates who demonstrate academic leadership, independence, creativity and innovation in their work and foster a passion for future MND research
- to honour the memory and legacy of Angie Cunningham

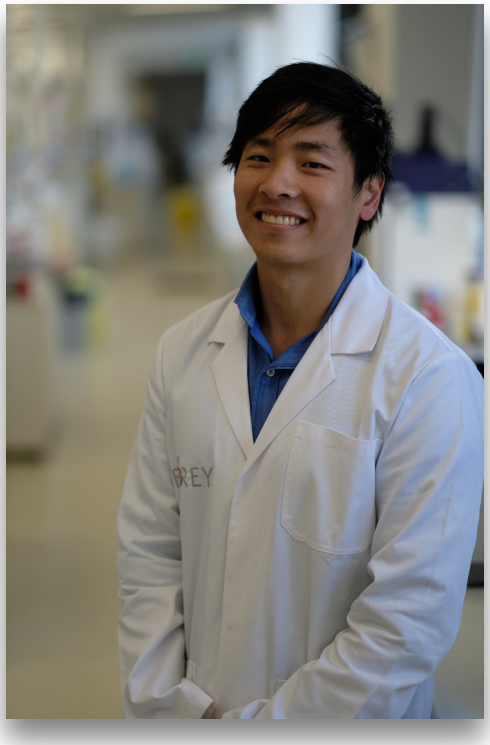
INAUGURAL ANGIE CUNNINGHAM PHD SCHOLARSHIP RECIPIENT

TED WANG

BLOCKING NECROPTOSIS-MEDIATED MOTOR NEURON DEATH IN MND

AWARD: $100,000 PER YEAR FOR 3.5 YEAR PROJECT

FLOREY INSTITUTE, MELBOURNE



MND is a complex disease involving interactions between many different cell types. There is increasing evidence that inflammatory cells called "astrocytes" which surround nerve cells contribute to motor neuron death and disease progression in MND. In particular, astrocytes trigger a cell death pathway called "necroptosis" in motor neurons, leading to loss of these nerve cells in MND. Importantly, astrocyte triggered necroptosis cell death occurs in both inherited and sporadic forms of MND. Necroptosis therefore offers a new and exciting potential therapeutic target for MND.

In this project, we will combine the use of world first and newly developed genetic and drug approaches to effectively target the necroptosis cell death cascade in MND. MND patient-derived cells will be treated with novel drugs which interfere with necroptosis to improve their health and survival. The lead compound will then be advanced to thorough evaluation in MND mice. We predict that blocking the necroptosis cell death pathway will improve motor neuron survival, motor co-ordination and lifespan in mouse models of MND. This will provide important "proof-of-principle" evidence that targeting the necroptosis cell death pathway is a meaningful and relevant approach for MND. These studies may encourage future development of strategies to effectively block necroptosis and protect motor neurons in MND.

Hypothesis

Inhibition of MLKL-dependent necroptotic signalling in motor neurons will counter astrocyte toxicity to motor neurons and improve motor function and survival in mouse models of ALS.

Aims

1. Determine the therapeutic effects of MLKL genetic ablation on symptom progression and neurodegeneration in mouse models of ALS.

2. Screen and prioritise novel MLKL inhibitors using ALS patient-derived motor neurons.

3. Determine the therapeutic effects of pharmacological inhibition of MLKL on symptom progression and neurodegeneration in mouse models of ALS

> **" FOR ME, TWO OF THE MOST INSPIRING QUALITIES THAT ANGIE HAD WERE HER TENACITY AND PERSEVERANCE FOR ALL THINGS IN LIFE. I THINK THOSE QUALITIES ARE ESSENTIAL FOR ANY STUDENT STUDYING FOR THEIR PHD...**