



Research Project  
By Dr Dorothy Wai



Dementia  
Australia  
Research  
Foundation

Bondi 2 Berry  
Dementia Research Grants



# Developing potent and brain-permeable peptide therapeutics for Alzheimer's disease



## What is the focus of the research?

Attempting to engineer a drug for Alzheimer's disease that can bypass the blood-brain barrier and enter the brain more efficiently.



## How will this happen?

**Stage 1:** Synthesise and characterise drugs that selectively target microglia and block its overactivated protein.

**Stage 2:** Attach 'shuttle' molecules to allow easier entry into the brain.

**Stage 3:** Test whether the shuttle-drug molecules can pass through a cell-based model of a blood-brain barrier.

**Stage 4:** Assess the ability of the shuttle drugs to enter the brain in mice.



## What is the Blood-Brain Barrier?

A critical immune cell type in the brain that normally protects neurons by clearing damage and debris. In Alzheimer's disease, microglia can become overactivated and damage neurons instead. Dr Wai's research aims to increase the brain delivery of a drug that specifically targets microglia, which may be able to prevent this damage to neurons.

## ! Why is it important?

Alzheimer's disease is a neurodegenerative disease that steals memories from people and causes significant heartache for family and friends in the process. It can also affect behaviour, language, judgement, mood, emotion, attention and thinking.

The fact that we know so little about such a devastating disease, and that it has no treatment, prevention or cure can be difficult for families to come to terms with. Despite numerous drug trials, there are currently no drugs that are able to slow the progression of Alzheimer's disease, and few that can even alleviate symptoms. One of the reasons so many drug candidates are ineffective is that too much of the drug is being blocked by the blood brain barrier. This tight protective barrier formed by blood vessels within the brain means the drugs are not reaching brain cells from the bloodstream.

It is vital that a method to deliver appropriate drugs across the blood-brain barrier are found, so that people living with dementia can receive long overdue treatments for this progressive disease.

## 👥 What will this mean for people with dementia?

- An opportunity to take part in clinical trials of a new potential drug candidate.
- Hope of an effective treatment for Alzheimer's disease.
- More diverse intervention options.

## ? What are Microglia?

A critical cell type in the brain. They're primarily an immune cell – so they are essential for proper functioning of nerve cells as well as for removing damage and debris in the brain. Using a drug candidate to specifically target microglia, Dr Wai may be able to block overprotective proteins to allow Alzheimer's drug treatments to be better delivered to the brain.

## 🕒 What will this mean for the future?

- A potent, selective and safe lead molecule that is ready for preclinical and clinical studies, and may ultimately be developed into a drug that suppresses neuroinflammation and slows cognitive decline in early or mild Alzheimer's disease.
- Knowledge of a therapeutically effective drug dose that can be delivered to slow Alzheimer's disease progression and preserve cognitive function.
- A therapeutic drug intervention that is cheaper and easier to produce than antibody-based therapies.
- Potential further applications for other microglial-linked disorders such as Parkinson's disease.



## Who's undertaking the research?

### Dr Dorothy Wai, Monash University

Dr Dorothy Wai is an early career postdoctoral researcher based at the Monash Institute of Pharmaceutical Sciences. Her research focuses on developing microglia-targeting peptides that have extended lifetime in the body and improved brain targeting for the treatment of neuroinflammatory conditions such as Alzheimer's disease.

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