



Treat

# Creating a healthy brain environment to treat Alzheimer's disease

RESEARCH PROJECT BY  
**Dr Simon Maksour**

## What is the focus of the research?

Developing a new treatment strategy for Alzheimer's disease that targets abnormally functioning immune cells in the brain.

## Why is this important?

Brain changes associated with Alzheimer's disease include a toxic build-up of proteins called amyloid beta and tau, and inflammation of immune cells called microglia. To date, treatment approaches have largely focused on removing the toxic proteins. Unfortunately, they are only mildly effective in slowing the progression of symptoms and have significant side effects. Thus, there is still no effective treatment or cure for Alzheimer's disease.

Dr Maksour hopes to uncover a new treatment approach by focusing on microglia, which are the brain's natural "clean-up crew".

They play an important role in maintaining the health of brain cells and clearing out toxic proteins, including amyloid beta.

In Alzheimer's disease, microglia do not function normally and this contributes to disease progression. Previously, approaches to improve microglia in Alzheimer's disease included transplantation of healthy microglia in mice. This improved cognition and protected against disease by reducing amyloid build-up. Unfortunately, while the microglia were effective, there were side effects that prevent it from being a suitable treatment strategy for Alzheimer's disease.

In this project, Dr Maksour will use an innovative gene therapy technology, called adeno-associated virus (AAV) vectors, to specifically deliver critical genes involved in restoring cell health to microglia and determine the effectiveness of this new therapy as a treatment option.

## Who's undertaking the research?



**DR SIMON MAKSOUR**  
**The University of Sydney**

Dr Maksour is a post-doctoral research Fellow at The University of Sydney. He is passionate about understanding the early cellular and molecular changes that occur in neurodegeneration, in the hopes of developing new treatments.

He utilises stem cells from people with neurodegenerative diseases to grow different types of brain cells in the lab to better understand changes that drive neurodegenerative diseases, so he can test new therapies.

The title of Dr Maksour's project is *Targeting Microglia as a novel treatment strategy for Alzheimer's disease*.

Dr Maksour and Dementia Australia Research Foundation would like to acknowledge Race Against Dementia for making this research possible.

## How will it happen?

### STAGE 1

Test over 80 different AAV vectors in microglia grown from people with Alzheimer's disease. The lead vectors will be validated to specifically and efficiently deliver genes to microglia in a petri dish.

### STAGE 2

Use the lead AAV vector to deliver critical genes to "mini-brains" grown from people with Alzheimer's disease and test whether the gene therapy can reduce inflammation, protect neurons from dying and reduce disease pathology.

### STAGE 3

Collaborate with researchers from the University of Antwerp, Belgium, to test the gene therapy in mice with Alzheimer's disease and determine whether the therapy can protect neurons from dying and slow disease progression and severity.

## What will this mean for the future?

- + A new treatment approach to slow Alzheimer's disease progression and severity, and protect the health of neurons and the brain.
- + Opens the door for combination therapies, using new or existing drugs for more personalised treatment.
- + The first-ever gene delivery system to target microglia that could be used for a multitude of inflammatory neurodegenerative diseases.