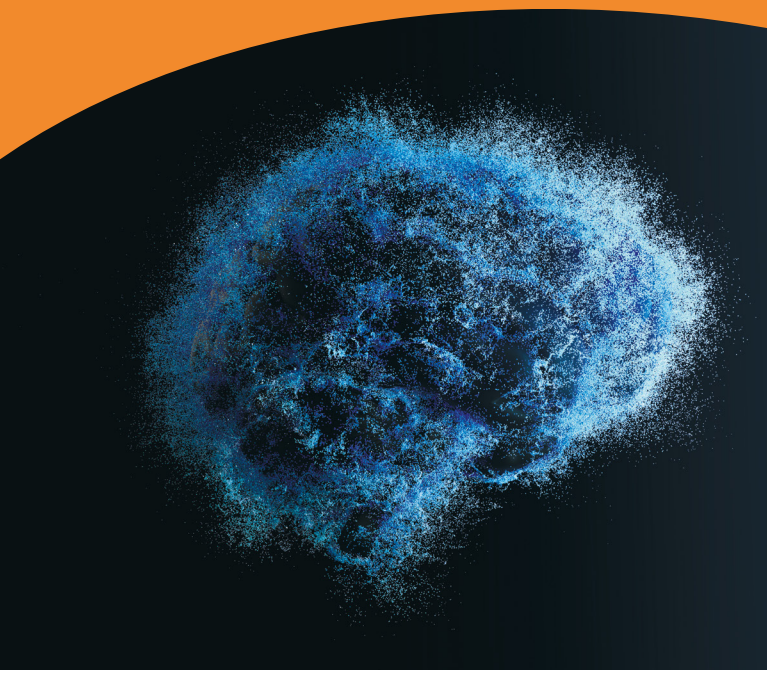
Research Project
By Dr Jereme Spiers

Dementia Australia Research Foundation

ROYCE SIMMONS FOUNDATION



> **Understanding how cells 'communicate' inflammation in the brain is critical in combating the progression of neurodegenerative diseases.**
>
> — Dr Jereme Spiers

# Targeting inflammatory brain particles to stop Alzheimer's disease progression

## What is the focus of the research?

Using cutting-edge technology to investigate whether targeting brain particles called extracellular vesicles (ECV) can stop Alzheimer's disease progression.

## Why is it important?

Ten million people around the world are diagnosed with dementia each year. The World Health Organisation called dementia "one of the greatest health challenges of our generation". The most common form, Alzheimer's disease, is progressive and fatal. Although scientists have some understanding of how it affects the brain, they still don't know enough about the disease's mechanisms to develop a cure or effective treatments.

The packaging of damaged, disease-promoting brain proteins into extracellular vesicles may be one cause of Alzheimer's disease progression. Extracellular vesicles are released by almost every cell in the human body and they help


cells communicate with each other. However, they have also been associated with multiple neurodegenerative disease processes, including neuroinflammation, which is a major contributor to all forms of dementia. In Alzheimer's disease, these vesicles may be spreading the damaged proteins and inflammation to healthy cells, causing its progression.

Until now, it hasn't been possible to study their potential disease pathways. In this project, Dr Spiers will use newly developed, ultra-sensitive techniques to obtain extracellular vesicles from healthy and Alzheimer's disease human brain tissue. He hopes to identify the specific types of brain cell these inflammatory vesicles originate from in Alzheimer's disease. For the first time, scientists will observe how extracellular vesicles contribute to disease, opening the door for the development of new treatments.

## How will this happen?

**Stage 1:** isolate ECV from the frontal cortex of human brains with and without Alzheimer's disease. Use specialised procedures to further separate these to identify which ones are responsible for neuroinflammation.

**Stage 2:** use a surface analysis to identify small changes in several different parts of the ECV, then use a type of artificial intelligence to sort these into meaningful targets for further analysis.

**Stage 3:** utilise a technique called proteomics to investigate how the ECV and toxic proteins interact. If Dr Spiers can identify a unique neuroinflammatory 'fingerprint' it will help him understand how they contribute to Alzheimer's disease.

## What will it mean for researchers worldwide?

- A new pathway for drug development.
- Better understanding of Alzheimer's disease mechanisms.
- The ability to adapt already-existing tools that target ECV to treat Alzheimer's disease.

## Extracellular vesicles, explained

Extracellular vesicles are membrane-bound particles that are secreted by cells into the extracellular space, which is a fluid-filled area surrounding our billions of cells. The fluid in this space contains substances that are important for healthy brain function. It's also an important cellular communication channel. There are different types of extracellular vesicles and they are essential in other physiological processes, such as metabolism, pregnancy and blood clotting. In Alzheimer's disease, scientists believe extracellular vesicles are spreading harmful proteins to healthy cells via the extracellular space channel.

## Who's undertaking the research?

**Dr Jereme Spiers, Australian National University**

Dr Spiers is a neuroscientist investigating the relationship between neuroinflammation, oxidative stress and neurodegeneration. Following his PhD, he was recruited to the Medical Research Council Toxicology Unit in the United Kingdom, where he investigated neuroinflammatory neurodegeneration in prion disease. He then joined La Trobe University where he began studying extracellular vesicles. Here, he investigated how they contribute to neuroinflammation in neurodegenerative diseases. Dr Spiers recently joined the Australian National University, where he aims to develop neuroinflammatory 'fingerprints' in neurodegenerative diseases.

The title of Dr Spiers' project is *Neuroinflammatory profile of microglial extracellular vesicles in Alzheimer's disease.*

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