



Understand

# Piecing together the role of protein interactions in the Alzheimer's disease puzzle

RESEARCH PROJECT BY  
**Dr Annika van Hummel**

## What is the focus of the research?

This research will investigate how a protein called TDP-43, that has recently been discovered to be involved in Alzheimer's disease, contributes to the progression and severity of disease by examining how it interacts with other Alzheimer's related proteins.

## Why is this important?

Most medicines for Alzheimer's disease have so far failed, likely because they tend to address only one aspect of disease. Alzheimer's disease, however, presents in different ways in different patients, making it more difficult to treat.

Up until recently, two proteins called tau and amyloid-beta (found in all Alzheimer's disease brains) have been thought to be the main contributors to the disease. A third protein, called TDP-43, has been recently found in a

large proportion (up to 70%) of patient brains, and has been linked to more severe disease. However, its role in disease progression is currently unknown.

Understanding how this protein contributes to disease, and how it interacts with other disease-related proteins (tau and amyloid-beta) will help researchers to understand the bigger picture of what is going on in the brain in Alzheimer's disease. This will in turn lead to better options for treating a wider range of people living with different presentations of Alzheimer's disease.

## What is TDP-43?

TDP-43 is a protein that is crucial for normal brain cell function. It plays a significant role in motor neuron disease and frontotemporal dementia. During disease, TDP-43 acts abnormally, changes its structure and clumps together which blocks important cell processes. This means it is unable to perform its normal cell functions and becomes toxic.

## Who's undertaking the research?



**DR ANNIKA VAN HUMMEL**  
**Macquarie University**

Dr Annika van Hummel is a Senior Research Fellow at the Dementia Research Centre at Macquarie University. For the last decade, her research has focused on understanding disease processes in neurodegenerative diseases and testing novel therapeutics using genetically modified mouse models. Dr van Hummel is particularly passionate about understanding the role TDP-43 plays in motor neuron disease, frontotemporal dementia and Alzheimer's disease, and works collaboratively within the multi-disciplinary team at the Dementia Research Centre to develop and test new therapeutic approaches to disease treatments.

Dr Annika van Hummel's research project is titled Piecing Together the Role of TDP-43 in the Alzheimer's Disease Puzzle.

## How will it happen?

### STAGE 1

**Understand how TDP-43 protein interacts with tau protein.**

Dr van Hummel will introduce diseased TDP-43 into mice that have been bred to have diseased tau protein in the brain to see if this accelerates and/or changes disease outcomes. This will be done by assessing symptom development (e.g. movement impairment and cognitive decline) and looking at brain cells over the course of disease to see how this compares to mice without diseased TDP-43.

### STAGE 2

**Understand how TDP-43 protein interacts with amyloid-beta protein.**

Similar to Stage 1, diseased TDP-43 will be introduced into mice that have been bred to have amyloid-beta plaques in the brain and again assess how this changes disease outcomes.

### STAGE 3

**Collection and Storage.**

Samples collected from these studies will be collected and stored for later experiments to identify new ways to detect people who are at risk of accelerated disease due to the presence of diseased TDP-43.

## What will it mean for dementia research?

- + A more thorough understanding of Alzheimer's disease progression and the different presentations of disease.
- + Potential for new treatments that target TDP-43 or interactions between TDP-43 and other proteins.
- + The presence of abnormal TDP-43 is not restricted to Alzheimer's disease, and findings may be applicable to other forms of dementia or neurodegenerative diseases.