



Understand

Unravelling mechanisms of tau in frontotemporal dementia

RESEARCH PROJECT BY
Dr Shanley Longfield

What is the focus of the research?

Exploring how a mutation in the protein tau, which is associated with frontotemporal dementia, alters brain structure and affects cellular communication. Using cutting-edge imaging techniques, it aims to reveal how these changes contribute to cognitive decline.

Why is this important?

Each year, millions of people are affected by frontotemporal dementia, a debilitating neurodegenerative disorder and a leading cause of younger-onset dementia. Unfortunately, there is no cure. Tau is important for healthy brain function. But in frontotemporal dementia, it mutates and disrupts areas of the brain responsible for memory, language and behaviour. However, scientists still don't understand the exact mechanisms of how mutated tau causes cognitive decline.

Recent discoveries show that healthy tau controls the clustering of synaptic vesicles within neurons. This helps regulate communication between brain cells,

which is a crucial part of brain functioning. However, when this process goes awry, it may contribute to diseases like frontotemporal dementia.

By using state-of-the-art super-resolution microscopy, Dr Longfield will investigate how mutated tau impacts brain function. Her goal is to uncover what goes wrong in frontotemporal dementia at a molecular level and explore potential ways to protect brain cells from damage, offering hope for better treatments in the future.

The synapse and synaptic vesicles, explained.

The synapse is the space between brain cells (neurons) that allows them to communicate with each other via chemical signals. Synaptic vesicles are small reservoirs within neurons that are filled with these chemical signals (neurotransmitters). When a neuron gets activated, electrical signals tell these synaptic vesicles to release their neurotransmitters into the synapse to activate another neuron. This is how information is passed around the brain.

Who's undertaking the research?



DR SHANLEY LONGFIELD
The University of Queensland

Dr Longfield is a post-doctoral research fellow at the Queensland Brain Institute, The University of Queensland. Her research explores the molecular mechanisms regulating synaptic function in neurological disorders.

Using cutting-edge genomic techniques, she investigates synaptic proteins that control neurotransmitter release at the nanoscale level. Through this work, Dr Longfield aims to enhance the understanding of synaptic dysfunction and contribute to the development of innovative therapeutic strategies.

The title of Dr Longfield's project is *Unravelling nanoscale dynamics and dysfunction of tau in frontotemporal dementia*.

Dr Longfield and Dementia Australia Research Foundation would like to acknowledge Dementia Research Community for making this research possible.

What is tau?

Tau is a key brain protein that binds cellular structures and supports their stability. In dementia, it misfolds and forms toxic aggregations, disrupting brain function and driving memory loss. Understanding and targeting tau is crucial for developing breakthrough treatments to slow or stop neurodegeneration.

How will it happen?

STAGE 1

Track tau in living neurons.

Super-resolution single-molecule tracking microscopy will be used to track tau molecules and examine how the frontotemporal dementia-linked mutation affects tau's nanoscale organisation in live neurons. By comparing normal and mutated tau, changes in its organisation at the synapse will be identified.

STAGE 2

Investigate the impact on synaptic vesicles.

Dr Longfield will use single-molecule imaging to track how mutated tau affects synaptic vesicle clustering, which is essential for maintaining neurotransmitter release. Changes in vesicle clustering and mobility will be analysed to determine how tau mutations disrupt neuron communication, contributing to frontotemporal dementia progression.

What will it mean for research?

- + Important insights into tau's synaptic function and dysfunction in frontotemporal dementia, increasing researchers' understanding of its role in neurodegenerative diseases..
- + Advancing cutting-edge imaging techniques to study neurodegenerative diseases at a nanoscale level.
- + Leading to the development of new, targeted treatments for disease progression aimed at correcting tau-related dysfunctions in neurodegenerative diseases.