Research project by
Dr Pradeep Manuneedhi Cholan

RACE AGAINST DEMENTIA

Dementia Australia Research Foundation

Treat

Gut-brain connection holds promise for Alzheimer's disease treatment

What is the focus of the research?

Investigating how changes in the microbiome can increase Alzheimer's disease risk – and how our own gut bacteria can be used to develop groundbreaking treatments.

Why is this important?

The gut is often referred to as our 'second brain' as it can control our emotions, stress response and cognition.

It's also a powerful organ that has a controlling influence on the immune system. Pioneering research has discovered a connection between a dysfunctional gut and Alzheimer's disease. Bacterial species in the gut can regulate inflammation in the brain and either exacerbate or alleviate disease progression.

Excitingly, this new understanding of the gut-brain connection has uncovered the potential for world-class researchers, such as Dr Cholan, to develop gut-directed treatments. Dr Cholan will study the microbiome in the faeces of people living with Alzheimer's disease to generate critical new insights that could pave the way for pioneering treatments to become a reality.

Microbiome, explained

Microbiome is the trillions of microorganisms that live inside the gastrointestinal tract. It consists of good and bad bacteria, fungi and viruses. An imbalance in this important ecosystem may lead to systemic and neuronal inflammation, which can break down the blood-brain barrier and damage the brain.

He's also aiming to develop approaches that lead to early and non-invasive diagnosis via stool sample testing. If successful, this project will pave the way for early diagnosis, new drug treatments and lifestyle interventions that prevent or manage Alzheimer's disease.

How will it happen?

Stage 1: transplant faecal matter of people living with Alzheimer's disease into zebrafish. Observe their brain cells and guts for signs of inflammation. Monitor their behaviour and stress response to stimuli such as light.

Stage 2: analyse and compare metabolites (bacterial by-products) in diseased and healthy faeces to identify specific metabolites that could be used to treat Alzheimer's disease. Transplant those metabolites into zebrafish and observe the impact this has on their guts and brains.

Stage 3: feed mice bred to have aspects of Alzheimer's disease three of the metabolites identified in stage two. Monitor their memory and movement, comparing them with healthy mice. Examine their brains and spinal cords for signs of Alzheimer's disease to see if those metabolites slowed disease progression.

What will it mean for the future?

- Early and non-invasive diagnoses of Alzheimer's disease.
- Potential for new drug treatments that prevent or slow disease progression.
- A new understanding of how lifestyle influences disease risk.

Why zebrafish?

Zebrafish are transparent when young, which makes it easy for researchers to observe their fluorescent cells. They can see, in real time, how the bacteria affect inflammation in the gut and brain.

Who's undertaking the research?

Dr Pradeep Manuneedhi Cholan, Macquarie University

Dr Cholan is a post-doctoral research fellow in the Motor Neuron Disease Research Centre at Macquarie University. He investigates molecular and cellular pathways affected in neurodegeneration, with a focus on the role of gut microbiome in neurodegenerative diseases. Dr Cholan is passionate about designing and developing high-throughput models to aid in drug discovery.

The title of Dr Cholan's project is *Identifying the effects of the gut microbiome on microglial cells in Alzheimer's disease*.

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