Research project by
Dr Janet van Eersel

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Treat

One step closer to a treatment that targets the build-up of toxic protein in the brain

What is the focus of the research?

Developing a next-generation dementia treatment that acts on the abnormal build-up of a protein called tau within brain cells that causes cognitive decline.

Why is this important?

The project utilised cutting-edge technology to transform the development of future dementia treatments.

The abnormal clumping of tau is found in the brains of people with Alzheimer's disease and frontotemporal dementia. At first, these clumps are small. But as disease progresses, they mature into large "neurofibrillary tangles", which scientists initially believed caused brain cells to die.

However, exciting new research suggests that it's the initial, smaller clumps that are responsible for cell death and subsequent cognitive impairment.

This discovery had major implications, since drugs that are currently in clinical trials are designed to target and dissolve the mature neurofibrillary tangles. These drugs may cause the release of the small, toxic tau clumps that were safely trapped away in mature tangles.

Dr van Eersel's project, commenced in 2020, aimed to create the next generation of tau-targeting drugs that act specifically on the smaller clumps, not the tangles.

Research stages?

Stage 1: tested a new lead chemical compound designed to prevent the formation of toxic tau clumps (without disturbing existing mature clumps) in genetically modified mice that develop tau pathology and exhibit dementia-like symptoms.

Stage 2: harvested mouse brains to assess any changes in the amount of tau clumping. Researchers continued refining the compound to achieve greater clinical results and generate new compounds.

What were the results?

- Developed a way of artificially generating small clumps of tau in the lab.
- Improved lab tests for better clump detection and experimentation.
- Identified drug compounds that act on small tau clumps.
- Identified potential new drug candidates for further development and entry into clinical trials, offering hope for better treatments for dementia.

What's next?

- Investigate how lab-grown tau behaves in mouse brains.
- Analyse how the drug prevents/ reduces tau clumps in mouse brains.
- If successful in mice, prepare for human clinical testing.

From mouse to man

Drug testing must undergo many rigorous phases of research before approval for use in humans. Mouse trials are within the "pre-clinical" phase. If a treatment is successful within this phase, there's still a long way to go before your doctor can write you a prescription. The drug candidate undergoes several more years of rigorous testing, so researchers can show it is safe and effective for use in humans. They then apply to the government's regulatory body, the Therapeutic Goods Administration, for approval to use in the next phase – human clinical trials.

There are four phases of clinical trials, which encompass the initial safety testing on a small group of people, through to studying the effectiveness of the drug and any adverse side-effects after it has been approved for public use. In general, it takes many years and billions of dollars for a drug to go from mouse trials to prescription pads.

Who's undertaking the research?

Dr Janet van Eersel, Macquarie University

Dr van Eersel is a group leader in the Dementia Research Centre in the Faculty of Medicine, Health and Human Sciences at Macquarie University.

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