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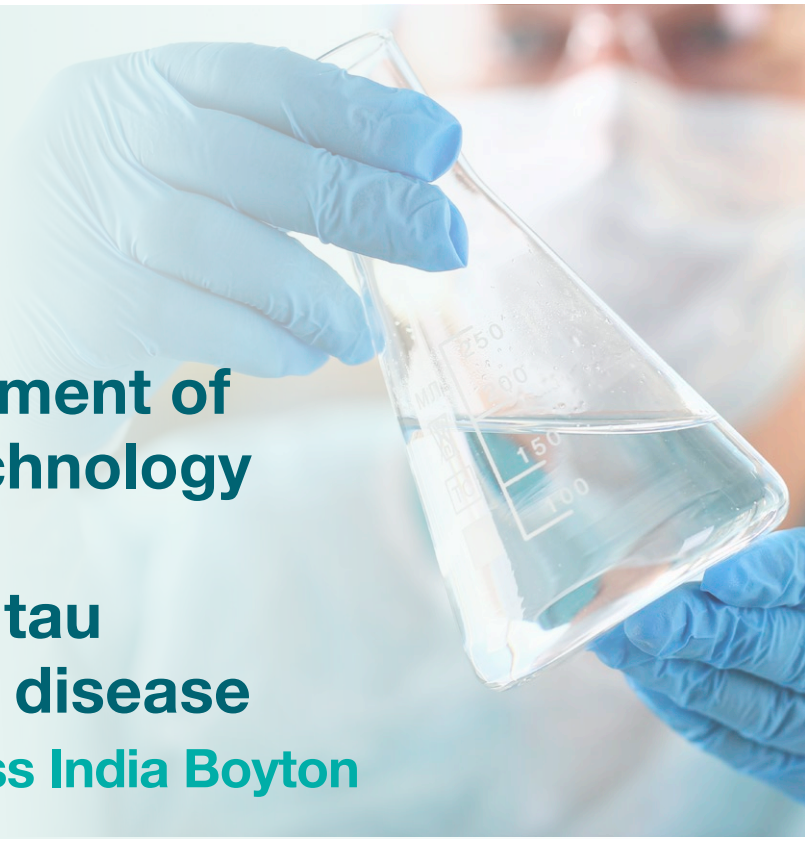

Cage vs Age: development of an innovative nanotechnology to halt the spread of hyperphosphorylated tau protein in Alzheimer's disease

by Dr Andrew Care and Miss India Boyton

What is the focus of the research?

To slow or stop the progression of Alzheimer's disease throughout the brain by engineering a biologically-derived nanotechnology that can target and disrupt extracellular pTau to significantly reduce its transmission.

How will this happen?

Stage 1: Determine the best biomechanistic properties and functions for a suitable nanocage platform, by investigating the criteria required to therapeutically target pTau.

Stage 2: Investigate the effect of the nanocage platform on braincell structure and function, and use Alzheimer's mouse models to test for toxicity.

Stage 3: Create an in vitro model to investigate the ability of the nanocage platform to selectively disrupt extracellular pTau and prevent or reduce cell-to-cell spread.

What is extracellular transmission?

Extracellular means outside the cell. In this project, Dr Care and Miss Boyton are particularly interested in the way pTau is transmitted when it's outside a cell, hence they use the term "extracellular transmission".

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Why is it important?

In recent years, researchers have discovered that a major contributor to the spread of Alzheimer's disease throughout the brain is the extracellular transmission of misfolded Tau proteins.

Current medications for Alzheimer's disease alleviate some symptoms for patients, but they do not modify the underlying brain mechanisms that cause this terrible disease. Therefore, there is only mild, short-term relief, and nothing to stop the inevitable and devastating cognitive decline of someone living with Alzheimer's disease as it continues to spread throughout their brain.

Whilst researchers have been investigating ways to clear the existing pTau for some time now, Dr Care and Miss Boyton are attempting a completely new approach through the invention of their "nanocage". They are attempting, for the first time, to specifically target the transmission of pTau, and in particular, target it in the extracellular space, which could neutralise its toxicity, isolate it from the disease pathway and stop it in its tracks. If successful, it could be used as an early intervention for people with Alzheimer's disease, and give hope to hundreds of thousands of Australians.

WHAT IS pTau?

Tau is a protein in the brain. When it undergoes abnormal phosphorylation (meaning something has been added to or modified in the Tau protein which changes the way it functions), it is then referred to as pTau.

A major contributor to the spread of Alzheimer's disease inside the brain is the transmission of these misfolded or abnormal forms of Tau (pTau). In this process, pTau is released from diseased brain cells and taken up by neighbouring healthy brain cells, triggering the misfolding of the normal Tau inside those cells too. Each time this happens, it is in effect creating more pTau and hence Alzheimer's disease progressively spreads throughout the brain.

What does Nano mean?

Nanotechnology is a science based on manipulating matter at the nanoscale – a very very tiny scale. A nanometre is so small in fact, it's only one-billionth of a metre.

At this level, unique phenomena are possible because this is the scale of molecules. By manipulating molecules, the most interesting things can happen - many that until recently, seemed impossible.

Nanoparticles are extremely small spheres that can be changed to package and target the delivery of drugs to a specific target within the body.

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What will this mean for people with dementia?

- A new and exciting way to slow or prevent the progression of Alzheimer's disease.
- A significant step towards the creation of a disease-modifying treatment for Alzheimer's disease.
- Real hope that there is light at the end of the tunnel.
- A reason to get tested and diagnosed early.

What will this mean for the future?

- A basis to translate the findings into pre-clinical models.
- Hope for sufferers of other neurodegenerative diseases, such as Parkinson's disease, thanks to a technology that could be readily adapted to disrupt other harmful proteins that drive the progression of these diseases.

What are biomechanistic properties?

Like other forms of mechanics, biomechanics looks at the mechanical aspects of a system. In the case of biomechanics, the cage system is a biological one, so it includes the effect the cage's physical structure has on its function.

In the case of *"Cage vs Age"*, it's important for the researchers to gain a very detailed understanding of the cage's properties and how they can be engineered to therapeutically target pTau. They test these "biomechanistic" properties in vitro (tests outside the body… think petri dishes and test-tubes) to make sure they get them just right.

Understanding the unique biomechanistic properties of the cage will help them re-engineer and then optimise the cage's functions, making it into a safe and effective nanotechnology system for when the cage becomes ready for use inside a human body.

Who's undertaking the research?

Dr Andrew Care, Macquarie University

Dr Care is a Cancer Institute NSW Early Career Fellow in the Department of Molecular Sciences at Macquarie University. His research combines techniques from synthetic biology and nanobiotechnology to engineer functional protein-based nanoparticles for the targeted delivery and controlled release of therapeutics in the treatment of diseases.

Miss India Boyton, Macquarie University

Miss Boyton is currently undertaking her PhD in Molecular Sciences at Macquarie University. She has already characterised the unique biomechanistic properties of a biologically-derived nanocage and will now re-engineer it to treat Alzheimer's disease.

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