Challenging long-held theories of Alzheimer's disease progression impacts future treatment options

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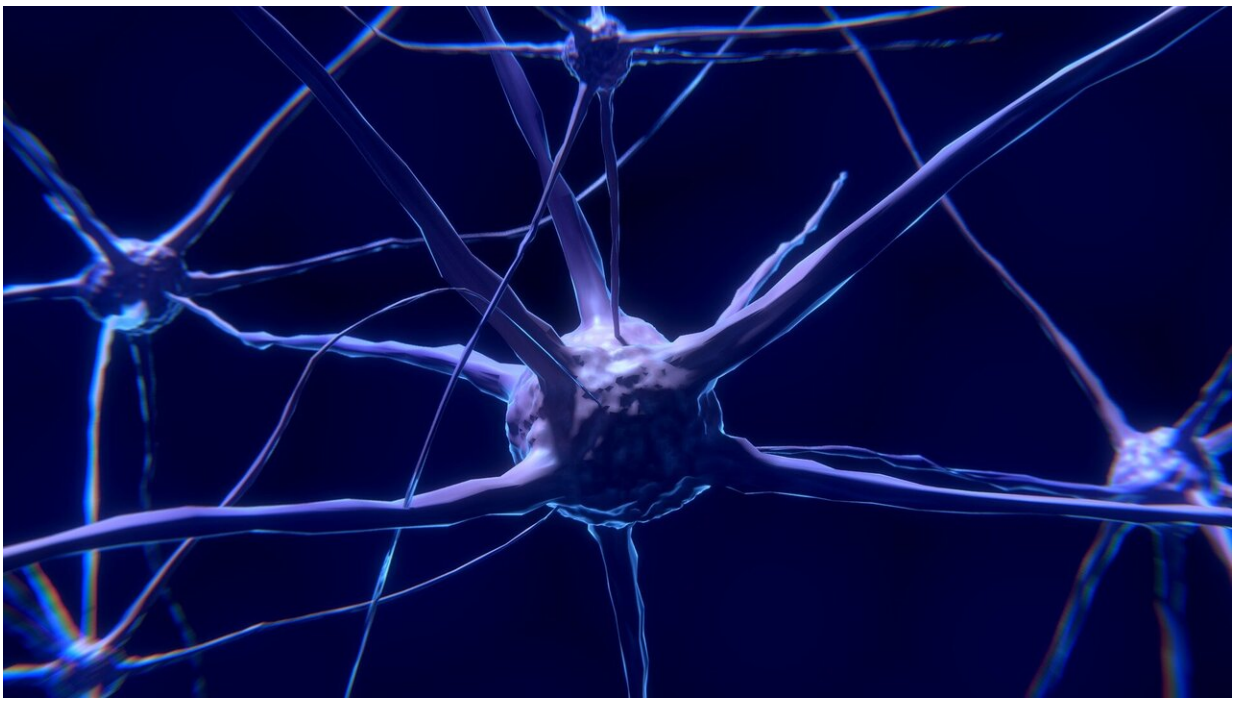

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Macquarie University dementia researchers have harnessed a system previously used for cancer research in a major discovery that debunks previous thinking on Alzheimer's Disease development.

The discovery will allow researchers to observe and analyze the life cycle of individual brain cells over time, including their response to potential new drug treatments.

The new findings reveal that mechanisms in brain cells, which were previously thought to be associated with cell death in Alzheimer's, appear to actually be providing a protective mechanism, resisting Alzheimer's Disease cell death and potentially prolonging progression of the disease.

The research paper, titled, "Rapid initiation of cell cycle reentry processes protects neurons from amyloid-β toxicity," has just been published in the prestigious *Proceedings of the National Academy of Sciences* (*PNAS*) journal, and paves the way for a radical rethink on how researchers approach their search for treatment of dementia.

"This method of study of the cell cycle, known as FUCCI, frequently used in cancer and developmental biology research, has not been used to study mature neurons in the context of neurodegenerative diseases," says lead author and founder of Macquarie University's Dementia Research Center (DRC), Professor Lars Ittner.

This builds on his team's work to discover a treatment for Alzheimer's Disease that began in 2016.

"A cell state that we so far believed to drive the disease is actually protecting the neurons. This opens up new research avenues, ideas and opportunities to harvest natural protective mechanisms for future dementia drug development," Professor Ittner says.

Crucial to the findings was the sharing of knowledge between Macquarie University's DRC and the University of Queensland Faculty of Medicine's Experimental Melanoma Therapy Group.

The co-senior-author of the study, University of Queensland cancer researcher, Professor Nikolas Haass has established and further developed a method to study cell cycle and cell death in cancer in real time. Using this approach, he can observe and analyze the fate of individual cells over time, for example in response to drugs or toxins. For this study, Professor Haass applied his expertise about the cell cycle behavior, which is considered unique in the field of neurobiology.

"This new research demonstrates that methodologies developed for research into one disease (cancer) can be extended to interdisciplinarily address other entities, such as Alzheimer's Disease."

"This discovery reveals the continued need to join forces where interdisciplinary barriers exist; without a cancer researcher involved we wouldn't have been able to get to this finding," Professor Ittner says.

The study provides a platform for Professor Ittner and his team to "venture into a new space" in dementia research, something he says they "would not have imagined possible."

More information: Stefania Ippati et al. Rapid initiation of cell cycle reentry processes protects neurons from amyloid-β toxicity, *Proceedings of the National Academy of Sciences* (2021). DOI: 10.1073/pnas.2011876118

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