Green tea and red wine extracts interrupt Alzheimer's disease pathway in cells

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Natural chemicals found in green tea and red wine may disrupt a key step of the Alzheimer's disease pathway, according to new research from the University of Leeds.

In early-stage laboratory experiments, the researchers identified the process which allows harmful clumps of protein to latch on to brain cells , causing them to die. They were able to interrupt this pathway using the purified extracts of EGCG from green tea and resveratrol from red wine.

The findings, published in the Journal of Biological Chemistry, offer potential new targets for developing drugs to treat Alzheimer's disease, which affects some 800,000 people in the UK alone, and for which there is currently no cure.

"This is an important step in increasing our understanding of the cause and progression of Alzheimer's disease," says lead researcher Professor Nigel Hooper of the University's Faculty of Biological Sciences. "It's a misconception that Alzheimer's is a natural part of ageing; it's a disease that we believe can ultimately be cured through finding new opportunities for drug targets like this."

Alzheimer's disease is characterised by a distinct build-up of amyloid protein in the brain, which clumps together to form toxic, sticky balls of varying shapes. These amyloid balls latch on to the surface of nerve cells in the brain by attaching to proteins on the cell surface called prions, causing the nerve cells to malfunction and eventually die.

"We wanted to investigate whether the precise shape of the amyloid balls is essential for them to attach to the prion receptors, like the way a baseball fits snugly into its glove," says co-author Dr Jo Rushworth. "And if so, we wanted to see if we could prevent the amyloid balls binding to prion by altering their shape, as this would stop the cells from dying."

The team formed amyloid balls in a test tube and added them to human and animal brain cells. Professor Hooper said: "When we added the extracts from red wine and green tea, which recent research has shown to re-shape amyloid proteins, the amyloid balls no longer harmed the nerve cells. We saw that this was because their shape was distorted, so they could no longer bind to prion and disrupt cell function.

"We also showed, for the first time, that when amyloid balls stick to prion, it triggers the production of even more amyloid, in a deadly vicious cycle," he added.

Professor Hooper says that the team's next steps are to understand exactly how the amyloid-prion interaction kills off neurons.

"I'm certain that this will increase our understanding of Alzheimer's disease even further, with the potential to reveal yet more drug targets," he said.

Dr Simon Ridley, Head of Research at Alzheimer's Research UK, the UK's leading dementia research charity, which part-funded the study, said: "Understanding the causes of Alzheimer's is vital if we are to find a way of stopping the disease in its tracks. While these early-stage results should not be a signal for people to stock up on green tea and red wine, they could provide an important new lead in the search for new and effective treatments. With half a million people affected by Alzheimer's in the UK, we urgently need treatments that can halt the disease – that

means it's crucial to invest in research to take results like these from the lab bench to the clinic."

More information: Jo V. Rushworth, Heledd H. Griffiths, Nicole T. Watt and Nigel M. Hooper, 'Prion protein-mediated neurotoxity of amyloid-β oligomers requires lipid rafts and the transmembrane LRP1,' *Journal of Biological Chemistry*, DOI:10.1074/jbc.M112.400358