

# 'Magic number' 695 opens up new areas for Alzheimer's research

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Alzheimer's disease is widely believed to be caused by the gradual accumulation in the brain of amyloid-beta peptide which is toxic to nerve cells. Amyloid beta peptide is formed from a protein known as APP, which is found in three forms. Most research into APP – a key area of study for the disease – does not distinguish between the different forms of the protein.

The findings, published in the *Journal of Biological Chemistry*, show that amyloid beta peptide is actually created mainly by just one form of APP – known as APP695 for the number of its amino acids. APP695 is found at greater concentration in brain and [nerve cells](#), but this study – funded by the Medical Research Council and the Alzheimer's Research Trust – is the first time the significance of that has been shown. This discovery will now enable research to focus more clearly on the exact mechanism by which amyloid beta peptide accumulates in the brain.

"Research into amyloid beta peptide has been going on for more than 20 years and while treatments have made it to clinical trials, nothing has proved truly effective against this disease," says Professor Tony Turner, from Leeds' Faculty of Biological Sciences, who co-led the research.

"This could be because research to date has been a bit of a blunt instrument: scientists have essentially been working on too broad a field. Our findings will allow researchers to target their work much more precisely."

The study of APP695 also led the scientists to identify a potential new

factor in the development of Alzheimer's. When APP is broken down, it forms another [protein](#) called AICD. The researchers discovered that AICD formed from APP695 switches on certain genes within nerve cells that may then damage the cell. The process is unique to nerve cells and AICD formed from the other forms of APP does not have this effect.

"AICD has been detected before, but because studies haven't differentiated between the different forms of APP, there was no consensus on its role," explains co-researcher Professor Nigel Hooper. "It seems likely that AICD formed from APP695 is a contributing factor in the deterioration in nerve and [brain](#) cells which leads to Alzheimer's. This provides another avenue for research into a potential cure for the disease."

Professor Chris Kennard, chair of the MRC Neurosciences and Mental Health Board, said: "This is the latest study from a long-term research collaboration to significantly further our understanding of neurodegenerative diseases, such as [Alzheimer's Disease](#). It forms part of a £4.1m investment by the MRC and is a shining example of where fundamental research, which unravels the complex biology of disease, can provide the building blocks for potential treatments in future."

Dr Simon Ridley, Head of Research at the Alzheimer's Research Trust, said: "This study gives us important new insight into the role of APP in Alzheimer's disease, and could have significant implications for future research in this area. We must now build on these findings with more research, as this is the only way we will be able to find an effective treatment for dementia."

Over 820,000 people in the UK live with dementia and one in three over 65s will die with some form of the disease. The Alzheimer's Research Trust estimates that the annual cost to the UK economy is £23 billion.

Provided by University of Leeds

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