

## A molecular chain reaction in Alzheimer's disease

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Researchers at Lund University in Sweden have identified the molecular mechanism behind the transformation of one of the components in Alzheimer's disease. They identified the crucial step leading to formations that kill brain cells.

Alzheimer's disease is associated with memory a loss and <u>personality</u> <u>changes</u>. It is still not known what causes the onset of the disease, but once started it cannot be stopped. The accumulation of plaques in the brain is widely considered a hallmark of the disease. The key discovery identified the chemical reaction that causes the plaques to grow exponentially.

Amyloid beta, a protein fragment that occurs naturally in the fluid around the brain, is one of the <u>building blocks</u> of plaques. However, the processes leading from soluble amyloid beta to the form found in the plaques, known as amyloid fibril, have not been known. In the very early part of the process, two <u>protein fragments</u> can create a nucleus that then grows into a fibril. In solution this is a slow process, but the rate can be enhanced on surfaces. The current study shows that fibrils present a catalytic surface where new nuclei form and this reaction increases the speed of the process. As soon as the first fibrils are formed, amyloidbeta fragments attach at its surface and form new fibrils that subsequently detach.

"This process is thus self-perpetuating, and autocatalytic, and the more fibrils are present, the quicker the new ones are created," says Sara



Snogerup Linse, Professor of Chemistry at Lund University and one of the researchers behind the study.

The findings also show that the chemical reaction on the fibril surface creates cell-killing formations. It is hoped that the research could lead to a new type of medication targeting early stages of the disease in the future.

The results have emerged from several years of laboratory work by Professor Snogerup Linse and her colleague in Lund, Erik Hellstrand, including development of extensive methods to obtain amyloid beta in highly pure form and to study its transformation in a highly reproducible manner. Additional methodology based on isotope labelling and spin filters was developed to monitor the surface catalysis and pin-point the origin of the forms that kill <u>brain cells</u>. The collaboration with the theoretical group and cell biologists at Cambridge University has been absolutely crucial for all the findings.

Provided by Lund University

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