Fruit flies and test tubes open new window on Alzheimer's disease

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A team of scientists from Cambridge and Sweden have discovered a molecule that can prevent a toxic protein involved in Alzheimer's disease from building up in the brain. Dr. Leila Luheshi, of the Department of Genetics at University of Cambridge, et al. found that in test tube studies the molecule not only prevents the protein from forming clumps but can also reverse the potentially toxic process. Then, using fruit flies engineered to develop a fly equivalent of Alzheimer's disease, they showed that the same molecule effectively "cures" the insects of the disease. This study will be published next week in *PLoS Biology*.

Alzheimer's disease is the most common neurodegenerative disorder and is linked to the misfolding and aggregation of a small protein known as the amyloid β (Aβ) peptide. Previous studies in animal models have shown that aggregation of Aβ damages neurons (a type of brain cell), causing memory impairment and cognitive deficits similar to those seen in patients with Alzheimer's disease. The mechanisms underlying this damage are, however, still not fully understood.

The new molecule - designed by scientists in Sweden - is a small protein known as an Affibody (a protein engineered to bind other proteins). In this new study, researchers at the University of Cambridge and the Swedish University of Agricultural Sciences found that in test-tube experiments this protein binds to the Aβ peptide, preventing it from forming clumps and breaking up any clumps already present.

In a second experiment, the authors studied the effect of this Affibody

in a Drosophila (fruit fly) model of Alzheimer's disease previously developed at the University of Cambridge. Working with genetically engineered fruit flies that developed the fly equivalent of Alzheimer's to produce the Aβ protein, they crossed these flies with a second line of flies genetically engineered to produce the Affibody. They found that offspring - despite producing the Aβ protein - did not develop the symptoms of Alzheimer's disease.

According to Dr. Luheshi "When we examined these flies we found that the Affibody not only prevented and reversed the formation of Aβ clumps, it also promoted clearance of the toxic Aβ clumps from the flies' brains."

"Finding a way of preventing these clumps from forming in the brain, and being able to get rid of them, is a promising strategy for preventing Alzheimer's disease. Affibody proteins give us a window into the Alzheimer's brain: by helping us understand how these clumps damage brain cells, they should help us unravel the Alzheimer's disease process."

According to Professor Torleif Härd of the Swedish University of Agricultural Sciences and one of the senior authors of the study "Our work shows that protein engineering could open up new possibilities in Alzheimer's therapy development."

More information: Luheshi LM, Hoyer W, Pereira de Barros T, van Dijk Ha¨rd I, Brorsson A-C, et al. (2010) Sequestration of the Aβ Peptide Prevents Toxicity and Promotes Degradation In Vivo. PLoS Biol 8(3): e1000334. doi:10.1371/journal.pbio.1000334

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