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Yeast model shows promise as Alzheimer's test

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A century ago this month, German psychiatrist Alois Alzheimer formally described characteristics of the neurodegenerative disease which ultimately came to bear his name. While international efforts to learn about Alzheimer's disease and develop treatments have progressed significantly in recent years, a cure remains an elusive goal.

A new research tool developed by Susan Liebman, distinguished university professor of biological sciences at the University of Illinois at Chicago, may ultimately provide a means for treating the earliest stage of Alzheimer's, thereby stemming its progression.

Alzheimer's disease is characterized by the formation of plaques in the brain largely composed of fibers made from a peptide called beta-amyloid, or A-beta, for short. There is abundant evidence to support the hypothesis that accumulation of A-beta peptide triggers the appearance of Alzheimer's. But while earlier research suggested the A-beta fiber caused Alzheimer's, recent research points at much smaller aggregates of the peptide as the culprit.

"We've developed a yeast model system in which A-beta small aggregate formation can be detected," said Liebman. "The system employs a fusion of the human A-beta peptide to a functional yeast protein, called a reporter protein, which is only active in allowing cells to grow on test media if the fusion does not form aggregates."

Liebman said the yeast model system can be used to develop a high

throughput assay to screen small molecules to find those that inhibit the A-beta dependent aggregation. "We'll screen a library of drugs and compounds, looking for ones that allow our yeast with the reporter protein to grow."

She said after the assay conditions are perfected, the screen will be ready for an automated process that will allow for fast testing of many compounds. Medicinal chemists would then study the structures of compounds that pass the screen and design compounds that enhance the activity without being toxic. Animal and human trials would follow.

"One promising, emerging approach for treatment of Alzheimer's disease is to prevent these smaller aggregates from forming," said Liebman. "Disruption of these small aggregates rather than the larger fibers seems prudent since inhibition of A-beta fiber formation might cause the smaller aggregate species to accumulate, and since inhibiting smaller aggregate formation should also prevent the initial formation of the fibers."

Source: University of Illinois at Chicago