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Anti-tau drug improves cognition, decreases tau tangles in Alzheimer's disease models

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While clinical trial results are being released regarding drugs intended to decrease amyloid production - thought to contribute to decline in Alzheimer's disease - clinical trials of drugs targeting other disease proteins, such as tau, are in their initial phases.

Penn Medicine research presented today at the 2012 Alzheimer's Association International Conference (AAIC) shows that an anti-tau treatment called epithilone D (EpoD) was effective in preventing and intervening the progress of Alzheimer's disease in animal models, improving neuron function and cognition, as well as decreasing tau pathology.

By targeting tau, the drug aims to stabilize microtubules, which help support and transport of essential nutrients and information between cells. When tau malfunctions, microtubules break and tau accumulates into tangles.

"This drug effectively hits a tau target by correcting tau loss of function, thereby stabilizing microtubules and offsetting the loss of tau due to its formation into neurofibrillary tangles in animal models, which suggests that this could be an important option to mediate tau function in Alzheimer's and other tau-based neurodegenerative diseases," said John Trojanowski, MD, PhD, professor of Pathology and Laboratory Medicine in the Perelman School of Medicine at the University of Pennsylvania. "In addition to drugs targeting amyloid, which may not work in advanced Alzheimer's disease, our hope is that this and other

anti-tau drugs can be tested in people with Alzheimer's disease to determine whether stabilizing microtubules damaged by malfunctioning tau protein may improve clinical and pathological outcomes."

The drug, identified through Penn's Center for Neurodegenerative Disease Research (CNDR) Drug Discovery Program, was previously shown to prevent further neurological damage and improve cognitive performance in animal models*. The Penn research team includes senior investigator Bin Zhang, MD, and Kurt Brunden, PhD, director of Drug Discovery at CNDR.

More information: Bristol-Myers Squibb, who developed and owns the rights to the drug, has started enrolling patients into a phase I clinical trial in people with mild Alzheimer's disease.

Presentation: "Microtubule Stabilizing Drugs for Abrogation and Prevention of Alzheimer's Disease," during symposium on "Insights into Non-Alzheimer's Disease Dementia Also Inform Us About Alzheimer's Disease"

*Brunden, K.R., Zhang, B., Carroll, J., Yao, Y., Poduzak, J.S., Hogan, A.M., Iba, M., James, M.J., Xie, S., Ballatore, C., Smith, A.B., III, Lee, V.M-Y., and Trojanowski, J.Q. Epothilone D improves microtubule density, axonal integrity and cognition in a transgenic mouse model of tauopathy. J. Neurosci., 30:13861-13866, 2010.

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