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New study identifies compounds that could slow down Alzheimer's disease

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A family of naturally occurring plant compounds could help prevent or delay memory loss associated with Alzheimer's disease, according to a new study by the Translational Genomics Research Institute (TGen).

Beta-carboline alkaloids could potentially be used in therapeutic drugs to stop, or at least slow down, the progressively debilitating effects of Alzheimer's, according to the study published recently in the scientific journal *Public Library of Science (PLoS) One*.

One of these alkaloids, called harmine, inhibits a protein known as DYRK1A, which has been implicated by this and other studies in the formation tau phosphorylation. This process dismantles the connections between brain cells, or neurons, and has been linked in past TGen studies to Alzheimer's disease.

Tau is a protein critical to the formation of the microtubule bridges in neurons. These bridges support the synaptic connections that, like computer circuits, allow brain cells to communicate with each other.

"Pharmacological inhibition of DYRK1A through the use of beta-carboline alkaloids may provide an opportunity to intervene therapeutically to alter the onset or progression of tau pathology in Alzheimer's disease," said Dr. Travis Dunckley, Head of TGen's Neurodegenerative Research Unit, and the study's senior author.

Beta-carboline alkaloids are found in a number of medicinal plants. They

have antioxidant properties, and have been shown to protect brain cells from excessive stimulation of neurotransmitters. "(They) are natural occurring compounds in some plant species that affect multiple central nervous system targets," the study said.

Under normal circumstances, proteins regulate tau by adding phosphates. This process of tau phosphorylation enables connections between brain cells to unbind and bind again, allowing neurons to connect and reconnect with other brain cells. However, this process can go awry, allowing the formation of neurofibrillary tangles, one of the signature indicators of Alzheimer's.

In this study, laboratory tests showed that harmine, and several other beta-carboline alkaloids, "potently reduced" the expression of three forms of phosphorylated tau, and inhibited the ability of DYRK1A to phosphorylate tau protein at multiple genetic sites associated with tau pathology.

"These results suggest that this class of compounds warrant further investigation as candidate tau-based therapeutics to alter the onset or progression of tau dysfunction and pathology in Alzheimer's disease," Dr. Dunckley said.

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