

Asthma drug could help control or treat Alzheimer's disease

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A drug used to treat asthma has been shown to help reduce the formation of amyloid beta, a peptide in the brain that is implicated in the development of Alzheimer's disease, according to researchers at Temple University's School of Medicine.

The researchers published their findings, "Pharmacologic Blockade of 5-Lipoxygenase Improves the Amyloidotic Phenotype of an AD Transgenic Mouse Model," in the [American Journal of Pathology](#).

In previous studies, the Temple researchers discovered that 5-lipoxygenase, an enzyme long known to exist in the [brain](#), controls the activation state of gamma secretase, another enzyme that is necessary and responsible for the final production of [amyloid beta](#). When produced in excess, amyloid beta causes neuronal death and forms plaques in the brain. The amount of these [amyloid plaques](#) in the brain is used as a measurement of the severity of Alzheimer's.

In their current study, led by Domenico Praticò, an associate professor of pharmacology in Temple's School of Medicine, the researchers tested the drug Zileuton, an inhibitor of 5-lipoxygenase typically used to treat [asthma](#), in a transgenic mouse model of [Alzheimer's disease](#). At the end of the treatment they found that this drug, by blocking the 5-lipoxygenase, reduced gamma secretase's production of amyloid beta and the subsequent build up of amyloid plaques in the brain by more than 50 percent.

Praticò said that gamma secretase is present throughout the body and, despite its role in the development of amyloid plaques, plays a significant role in numerous important functions. Direct inhibitors of gamma secretase are known, he said, but blocking the enzyme completely may cause problems such as the development of cancer. Unlike classical gamma secretase inhibitors, Zileuton only modulates the protein expression levels, which keeps some of its vital functions in tact while blocking many of its bad effects, which in this case is the development of the amyloid plaques.

Praticò and his colleagues have begun working with researchers in Temple's Moulder Center for Drug Discovery Research to create more potent inhibitors that can target 5-lipoxygenase in the [brain](#) and increase the ability to reduce amyloid plaque formation and the development of Alzheimer's. Because Zileuton is already FDA approved, it is known that 5-lipoxygenase inhibition is an acceptable target that is not associated with overt toxicity and therefore not harmful to patients. The new drug derivative might be expected to advance to clinical trials relatively easily.

"This drug is already on the market and, most importantly, is already FDA-approved, so you don't need to go through an intense drug discovery process," said Praticò. "So we could quickly begin a clinical trial to determine if there is a new application for this drug against a disease where there is currently nothing."

Provided by Temple University

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