

Drug restores cells and memories in Alzheimer's mouse models

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Cortical tissue with plaques stained in blue, and astrocytes responding to drug treatment in red. Credit: Yale University

A new drug can restore memories and connections between brain cells in mice with a model of Alzheimer's disease, a new Yale-led study suggests.

"The drug completely erased evidence of Alzheimer's synapse damage and memory loss in mouse models of the disease," said Stephen Strittmatter, the Vincent Coates Professor of Neurology and senior author of the study appearing July 5 in the journal *Cell Reports*.

Researchers such as Strittmatter have made significant inroads into understanding the biology of Alzheimer's disease, but identifying effective and

safe treatments has been difficult. It is known that amyloid-beta peptides, the hallmark of Alzheimer's, couple with prion protein at the surface of brain <u>cells</u> and transmit damaging instructions to the interior of the cell. Yale researchers had previously identified a protein on the cell membrane—metabotropic glutamate receptor 5 or mGluR5—as the gateway that helps transmit damage from the coupling.

Previous attempts had been made to target mGluR5, but most drugs also disrupt signaling of glutamate, the most common neurotransmitter in the human brain. The new compound, Silent Allosteric Modulation or SAM (BMS 984923), was created by Bristol Myers Squibb as part of its effort to treat schizophrenia. The drug does not restrict neurotransmitter signaling in culture tissue or living mice, the study found. After four weeks of treatment, memory and synapses linking <u>brain cells</u> had been restored in mice with a model of Alzheimer's.

"The drug does not destroy plaques associated with Alzheimer's, but allows them to co-exist with neurons," Strittmatter said.

Yale researchers say the next step is to prepare for preliminary trials of the drug's effects on humans.

Provided by Yale University



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