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## Protein Restores Learning, Memory in Alzheimer's Mouse Model

*Scientists at the UT Health Science Center San Antonio restored learning and memory in an Alzheimer's disease mouse model by increasing a protein called CBP. Salvatore Oddo, Ph.D., of the university's Department of Physiology and Barshop Institute for Longevity and Aging Studies, said this is the first proof that boosting CBP, which triggers the production of other proteins essential to creating memories, can reverse Alzheimer's effects.*

The finding, reported this week in Proceedings of the National Academy of Sciences, provides a novel therapeutic target for development of Alzheimer's medications, Dr. Oddo said. Alzheimer's and other dementias currently impair 5.3 million Americans, including more than 340,000 Texans.

### Alzheimer's Pathology

In patients with Alzheimer's disease, accumulation of a protein called amyloid- $\beta$  (A $\beta$ ) blocks memory formation by destroying synapses, the sites where neurons share information. Autopsies of the brains of some Alzheimer's patients also reveal tangles caused by a protein called tau.

Enhancing CBP does not alter the A $\beta$  or tau physiology but operates on a different recovery mechanism: It restores activity of a protein called CREB and increases levels of another protein called brain-derived neurotrophic factor (BDNF).

### Enhancing Signals

"One way by which CBP could work is by setting off a domino effect among proteins that carry signals from the synapse to the nucleus of the neuron," Dr. Oddo said. "Getting signals to the nucleus is necessary for long-term memory."

### A Viral Vehicle

The research team engineered a harmless virus to deliver CBP to the hippocampus in the temporal lobe. The hippocampus is the brain's key structure for learning and memory. At 6 months of age, when the CBP delivery took place, the specially bred mice were at the onset of Alzheimer's-like deficits. Learning and memory were evaluated in a water maze that required mice to remember the location of an exit platform. The mice treated with CBP were compared to diseased mice that received only placebo and to normal, healthy control mice.

### Identical to Healthy Mice

Efficiency in escaping the maze served as signs of learning and memory. In the Alzheimer's mouse model, performance of the Alzheimer's mice treated with enhanced CBP was identical to the healthy mice, whereas the placebo-treated Alzheimer's mice lagged far behind.

Antonella Caccamo, Monica A. Maldonado, Alex F. Bokov, Smita Majumder and Salvatore Oddo. CBP gene transfer increases BDNF levels and ameliorates learning and memory deficits in a mouse model of Alzheimer's disease. PNAS, December 13, 2010 DOI: 10.1073/pnas.1012851108