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Newly identified antibodies effectively treat Alzheimer's-like disease in mice

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Alzheimer's disease is characterized by the accumulation of particular toxic proteins in the brain that are believed to underlie the cognitive decline in patients. A new study conducted in mice suggests that newly identified antibody treatments can prevent the accumulation of one of these of these toxic components, called tau proteins. The findings, online September 26 in the Cell Press journal *Neuron*, suggest that these antibodies may provide a basis for a promising therapy for patients with Alzheimer's disease and other neurodegenerative disorders.

In the brains of patients with Alzheimer's disease and several other neurodegenerative conditions, tau proteins aggregate together and become tangled, a process that interferes with the brain's function and can cause many of the symptoms that patients experience.

Investigators led by Drs. David Holtzman and Marc Diamond of Washington University School of Medicine in St. Louis conducted studies in mice to reveal potential treatments to block this process. "We have identified anti-tau antibodies that can strongly reduce tau pathology, decrease tau accumulation, and improve cognitive function in a mouse model of a neurodegenerative disease called frontotemporal dementia," explains Dr. Holtzman. "Similar tau pathology is seen in Alzheimer's disease, implying that this could be an exciting treatment for a large number of patients."

To make their discovery, the researchers used a screening technique to sift through numerous antibodies to isolate those that could prevent

uptake of tau aggregates by cells and block subsequent intracellular tau aggregation. They then infused three anti-tau antibodies into the brains of diseased mice over three months. While the anti-tau antibodies markedly reduced tau accumulation and improved cognitive deficits in the animals, a control antibody not directed against tau had no beneficial effects. The findings further support work suggesting that spread of tau aggregates between cells is an important mechanism underlying tau-mediated disease.

This study, which is the first to report the effects of direct infusion of anti-tau antibodies into the brain, has important implications for the design of therapeutic antibodies for patients struggling with some of the most debilitating brain diseases. "In addition to the near-term implications for passive vaccination of patients, it suggests that therapies designed to target propagation of protein aggregation between cells could be very effective," says Dr. Diamond.

More information: *Neuron*, Yanamandra et al.: "Anti-tau antibodies that block tau aggregate seeding in vitro markedly decrease pathology and improve cognition in vivo." dx.doi.org/10.1016/j.neuron.2013.07.046

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