pT181-Qβ vaccine reduces pathological Tau and rescues cognitive deficits in a mouse model of tauopathy

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Title:

pT181-Qβ vaccine reduces pathological Tau and rescues cognitive deficits in a mouse model of tauopathy

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Abstract:
Alzheimer’s disease (AD), which currently affects 5.7 million people in the US, is clinically characterized by progressive memory decline. Since aging is a primary risk factor, and we are all getting older, this number is expected to triple to nearly 16 million, signaling a troubling health crisis. Tau, a protein in the brain, which normally provides support within neurons changes during the course of AD into pathological tau (pTau). pTau then accumulates as insoluble tangles within neurons, causing cell death, brain atrophy, and memory impairment. In the current study, we have developed a vaccine using a virus-like particle (VLP) platform targeting a type of p-Tau commonly seen in human patients, (pT181). Our VLP vaccine, derived from a bacteriophage called ‘Qβ’, contains a high density of viral coat proteins to which pT181 can easily adhere. Our vaccine, pT181-Qβ, works through B-cells, turning these potent immune cells into antibody producing factories. In order to test the efficacy of our novel vaccine, we used a humanized tau mouse model of tauopathy (rTg4510) and injected pT181-Qβ (our vaccine) and Qβ (control), bi-weekly for 6 weeks. First, we observed a robust and long-lived antibody response against p-T181 in the serum and brains of pT181-Qβ vaccinated mice, which were specific for pathological species of tau. Next, antibodies generated by pT181-Qβ reduced both soluble and insoluble species of pTau, in the brain, decreased brain atrophy, and prevented neuronal cell death. Overall, the VLP vaccine, pT181-Qβ, rescued cognitive dysfunction by decreasing levels of pTau and tau tangles while simultaneously preventing cell death. Therefore, VLP-based vaccination represents an exciting new avenue for drug development against AD.