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(54) **Title**: PROTEIN-BASED THERAPY AND DIAGNOSIS OF TAU-MEDIATED PATHOLOGY IN ALZHEIMER'S DISEASE

(57) **Abstract**: The invention provides unique therapeutic and diagnostic antibodies, as well as their fragments, portions, derivatives, and variants thereof, that bind regions of the tau protein that contribute to the initiation and propagation of pathological tau-tau interactions, as well as methods of making them. The invention also relates to methods of using those antibodies for diagnostics, prevention, and treatment of Alzheimer's disease and related tauopathies. The present invention also provides a method for a prophylactic and therapeutic treatment of Alzheimer's disease and other neurodegenerative tauopathies. This method entails the injection of antibodies and/or peptide vaccines that elicits an immune response directed to pathological tau proteins and tau deposits in the brains of patients. Suitable vaccines represent a tau peptide carrying one or more of the tau therapeutic epitopes provided herein.

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