

CTAD Highlights November 16, 2013

San Diego, California. Increased focus on the protein tau as an important player in Alzheimer's disease (AD) continued on the last day of the sixth annual Clinical Trials in Alzheimer's Disease (CTAD) conference. Tau is the protein that aggregates as neurofibrillary tangles, leading to the degeneration of neurons, in the brains of people with AD and other dementing diseases known collectively as "tauopathies". These diseases include progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), certain forms of frontotemporal dementia (FTD) and chronic traumatic encephalopathy (CTE), the type of dementia that has been associated with traumatic brain injury.

Over the past few years, a new hypothesis has emerged to explain how aggregated tau may lead the progressive dementia that characterizes AD. The mechanism involves the spreading of misfolded and aggregated tau from cell to cell and from one part of the brain to another, where it where it acts in a "prion-like" fashion to seed further aggregation.

The idea that aggregated tau forms in cells, escapes, and seeds adjacent cells not only helps explain how pathology progresses throughout the brain over time, but also gives rise to a new therapeutic strategy, said David Holtzman, M.D., Professor and Chair of Neurology at Washington University in St. Louis, Missouri. "If that's occurring, you might be able to stop that process in the extracellular space," for example with an antibody against tau that could prevent cell-to-cell spread.

Dr. Holtzman has been working with Marc Diamond, also at Washington University, to study tau metabolism in the brain. They have also created a series of antibodies against both soluble and aggregated forms of tau. Several of these antibodies block the ability of aggregated forms of tau to enter cells and seed aggregation of tau in vitro; and reduces the development of tau pathology in mice that have been engineered to express a mutant form of human tau that causes early onset FTD. Untreated, these mice develop tau aggregates in the brain at about 6 months and brain shrinkage by 8 months. These data suggest that anti-tau antibodies may represent a promising strategy for the treatment of tauopathies, including AD.

The data that Dr. Holtzman presented at CTAD drew enthusiastic responses from industry and academic attendees in the audience. Dr. Holtzman emphasized, however, that many questions remain unanswered. "We know so little about the mechanism of how these things are working and we need to do a lot more studies," he said.