Donna Wilcock, Ph.D.
Duke University Medical Center
Durham, North Carolina

A Study to Validate Tau as a Therapeutic Target for Alzheimer’s Disease
2009 New Investigator Research Grant

Tau is a protein that normally functions as part of a nerve cell’s internal structure. In Alzheimer’s disease, however, tau becomes abnormally modified by the addition of phosphate groups, a process known as hyperphosphorylation. Hyperphosphorylated tau forms neurofibrillary tangles, which are one of the hallmark features of Alzheimer pathology.

With the goal of developing treatments to prevent or slow Alzheimer’s disease, scientists are testing numerous strategies. Two of the most prominent strategies involve preventing tau hyperphosphorylation and preventing accumulation of amyloid plaques, another hallmark feature of Alzheimer pathology. Indeed, one model of the disease process proposes that amyloid plaque triggers tau hyperphosphorylation.

Donna Wilcock, Ph.D. and colleagues are studying whether interruption of tau hyperphosphorylation is a viable strategy for treating Alzheimer’s disease. Using genetic techniques, they have developed a new strain of mice that exhibit the complete spectrum of Alzheimer-like pathologies, unlike previous model strains that exhibited only select features. Using this new strain, the researchers plan to test if neurodegeneration is prevented or slowed by drugs that reduce the hyperphosphorylation of tau. Dr. Wilcock’s team will assess the efficacy of these drugs by measuring amyloid plaques, neurofibrillary tangles, nerve cell death and cognitive function. These studies will help define the steps in the disease process that are most suitable as targets for drugs therapies.