

Chad A. Dickey, Ph.D.
University of South Florida
Tampa, Florida

Chemical Inhibition of Hsp70 as a Therapeutic Strategy for Alzheimer's Disease

2009 Investigator-Initiated Research Grant

The heat-shock proteins are a family of proteins that perform a number of important cellular functions, in addition to responding to conditions causing cellular stress. Heat-shock protein 70 (Hsp70) has been shown to increase the removal of the protein tau, the primary constituent of neurofibrillary tangles. Because neurofibrillary tangles are a characteristic feature of Alzheimer pathology, drugs that regulate the activity of Hsp70 may have potential as therapies for Alzheimer's disease and related disorders involving tau.

Chad A. Dickey, Ph.D. and colleagues have identified several chemical compounds that either inhibit or stimulate Hsp70 activity. Because of this effect, these compounds also influence the rate at which tau proteins are replaced in cells. The researchers now plan to study in detail the cellular effects of Hsp70 inhibitors and stimulators. They will perform studies in mice that have been genetically altered to express neurodegenerative pathologies related to abnormal tau. The researchers are interested in learning how modulators of Hsp70 activity affect the development of disease in these animals.

Dr. Dickey's team will also examine how different types of Hsp70 modulators, which act on different functions of the Hsp70 molecule, affect the function or removal of tau. Finally, they plan to examine how different modulators affect the interactions between Hsp70 and tau. These studies will help determine whether drugs that modulate Hsp70 activity are worth pursuing as potential therapies for Alzheimer's disease and related neurodegenerative disorders.