Researchers at the University of South Florida have identified a drug that may be used to treat patients who suffer from Alzheimer’s disease in order to prevent or slow down disease progression. Afobazole, a drug currently used in Russia to treat anxiety and panic disorders, has been shown to decrease injury in neurons and microglial cells caused by the toxic amyloid-beta (Aβ) fragment 25-35.

Alzheimer’s disease (AD) is a progressive neurodegenerative disorder that is the most common form of senile dementia in the United States. No therapy has been identified that can effectively halt or reverse its progression. Although the full pathophysiology underpinnings of AD remain elusive, one hallmark of AD is an increase in Aβ plaque formation in the brain. The Aβ fragment 25-35, which has been found in AD brains, has been proposed as a major contributor to the pathogenesis of AD. In addition, Aβ has been shown to initiate a sequence of events in microglial cells that ultimately produces neuronal death. This knowledge has generated considerable interest in identifying molecular targets for modulating the responses of these cells to Aβ and for regulating their contribution to AD pathology in general.

Our researchers have devised a method of treating Alzheimer’s disease using afobazole, a known anxiolytic compound. Afobazole has been identified as an agonist of sigma (σ) receptors, potential molecular targets that modulate multiple signaling and regulatory pathways. The activation of σ receptors by afobazole has been shown to mitigate Aβ25-35-induced microglial cell death as well as preserve functional responses of the microglial cells to ATP following Aβ25-35 exposure, which has significant implications for Alzheimer’s disease progression. Afobazole also effectively blocks microglial cell migration caused by Aβ25-35 while increasing their survival, which will facilitate clearance of the Aβ plaque. These properties and more make afobazole an attractive drug for potential Alzheimer’s therapeutics.

Advantages:
- Decreases microglial cell death
- Effective against Aβ toxicity
- Preserves functional responses of microglia to ATP after Aβ25-35 incubation

Current Technology Status:
Laboratory Testing Underway

Afobazole decreases microglial cell death produced by application of Aβ25-35: (A) Photomicrographs showing EthD-1 labeling (red) of microglial cells after a 72-hour incubation in media alone (i) or media w/ 25µM Aβ25-35 (ii), 30µM afobazole (Afob) (iii), or 30µM afobazole + 25 µM Aβ25-35 (iv). (B) Bar graph of the mean (±S.E.M.) relative number of apoptotic cells identified by EthD-1 labeling in multiple experiments when the cultures were incubated under the same conditions as A.