Researchers at the University of South Florida have developed a novel gene therapy for the treatment of age-associated neurodegenerative diseases.

Tauopathies including Alzheimer’s disease (AD) are comprised of age-associated neurodegenerative diseases. Tau stabilizes microtubules, but can aggregate from accumulation and posttranslational modifications. Currently, no disease modifying agents exist on the market for any of the tauopathies.

Arginine metabolism promotes significant consequences on cell physiology/pathology. One pathway leads to nitric oxide production by nitric oxide synthases (NOS), which can nitrate proteins and further cause aggregation. Other pathways lead to polyamines via Arg1 or arginine decarboxylase (ADC). Both nitric oxide and polyamines have been shown to modify disordered proteins such as tau, amyloid beta, and alpha synuclein. In mammalian systems, neurons may be sensitized to certain amino acids such as L-arginine, thus its depletion may trigger activation of autophagy or clearance of aggregated proteins.

Our inventor’s have successfully mammalianized, cloned, and expressed arginine deiminase (ADI) to deplete arginine without increasing either nitric oxide or polyamines. When overexpressed in the brain of tau transgenic mice, ADI significantly decreased tau pathology. Additionally, ADI reduced tau levels in cells that overexpress tau. This novel gene therapy by ADI may serve as a therapeutic target in reducing aggregation prone proteins such as tau, thus leading to a promising new treatment for age-associated neurodegenerative diseases.

ADVANTAGES:

- Decreases tau levels
- Metabolizes arginine
- Does not increase nitric oxide or polyamines

New Treatment for Neurodegenerative Diseases

AAV9-GFP

AAV9-ADIw

AAV9-Arginidine deiminase (ADI) overexpression in rTg4510 mice. AAV9-ADI (B) significantly reduced total levels (Tau H-150) in the brain compared to AAV9-GFP (A) controls.

Tech ID # 15A023