ATM (aurothiomalate) Inhibits aPKC in the Brain Mitigating the Effects of Hyperinsulinemia on Alzheimer's Pathology

Researchers at the University of South Florida have discovered a novel inhibitor of aPKC in the liver, aurothiomalate (ATM), mitigates the effects of hyperinsulinemia on Alzheimer’s pathology by unraveling the linkage mechanism between insulin resistance and neurodegenerative processes.

Advantages:

- The establishment of the linkage between two major diseases
- Discovery of a two-in-one inhibitor that reduces both insulin resistance-induced hyperinsulinemia and Alzheimer’s pathology

Breakthrough on the effects of hyperinsulinemia on Alzheimer’s pathology

Insulin-resistant obesity and metabolic syndrome are present in one of three adults and progress to type 2 diabetes mellitus (T2DM) in one of four people over 65 years of age. Alzheimer disease (AD) afflicts one of eight people above 65 years of age and one of two people above 85 years of age. Moreover, AD risk in people with T2DM and vice versa are increased two folds and fasting glucose intolerance or T2DM was present in four of five patients surveyed. It is therefore suspected that insulin-resistant states may predispose the brain to development of late-onset AD.

Our scientists have demonstrated how hyperinsulinemia provokes excessive increases in the activities of the protein kinases Akt and aPKC in the insulin-resistant brain and how this hyperinsulinization leads to increase in the levels of β-secretase activity and p-Tau which are associated with AD pathology.

Our inventors discovered that ATM effectively inhibits liver aPKC, diminishing systematic insulin resistance and hyperinsulinemia, which in turn prevents excessive activation of brain aPKC and Akt. By preventing the downregulation of factors needed for maintaining neuronal function and longevity, FOXOs and PGC-1α, and also preventing the upregulation of β-secretase, AD-associated Aβ and p-Tau; ATM ultimately restores normal central nervous system signaling, potentially preventing or assuaging AD pathology.