Researchers at the University of South Florida have invented a novel treatment for neurodegenerative diseases using aPKC inhibitors.

Insulin-resistant obesity is present in over 50% of people over the age of 50, and Alzheimer’s disease (AD) afflicts 45% of people over the age of 85. Moreover, clinical data of a group of AD patients found that 80% of them have Type 2 Diabetes Mellitus (T2DM) or pre-diabetes. It is therefore speculated that insulin resistance increases AD susceptibility, and our inventors indeed found that insulin signaling to Protein Kinase B (Akt), atypical Protein Kinase C (aPKC), and to various Akt substrates was maximally increased in the brains of multiple insulin resistant animal models. They also found that increased blood insulin was responsible for observed alterations in CNS signaling factors. Hence, Hyperinsulemia was established to be responsible for increases in factors that could reasonably lead to, or abet, development of the two major pathological processes that are characteristic of AD. i.e. tangles of phospho-Tau and plaques containing Aβ₁₄₀/₄₂. Ability to treat systemic insulin resistant disorders, and potentially related CNS cognitive disorders, in particular AD, is limited as most of the available insulin-sensitizers have only modest indirect effects on insulin induced alterations in the brain, and their effects on the brain and AD needs to be re-assessed in light of new findings, e.g. insulin and metformin activate brain aPKC thus unfortunately increase β-secretase activity and Aβ₁₄₀/₄₂ production.

With certain aPKC inhibitors and the right dose that crosses the blood-brain barrier, this approach can be used to specifically block aPKC and aPKC-dependent processes such as activation of β-secretase and subsequent increases in Aβ₁₄₀/₄₂ production. This treatment, therefore, has the ability to reverse the action of insulin and various other aPKC activators (anoxia, proinflammatory cytokines, lipids, alcohol) that induce or abet development of neurodegeneration, particularly AD. This direct CNS effect is in addition to effects of aPKC inhibitors that improve hepatic glucose and lipid metabolism, and thereby diminish hyperinsulinemia-induced aberrations in the CNS.

**ADVANTAGES:**

- Treats live to prevent hyperinsulemia
- Readily crosses Blood-Brain Barrier at low concentrations to block brain aPKC
- Reverses the ability of insulin and other aPKC activators to induce neurodegeneration by increasing activity of β-secretase and Aβ₁₄₀/₄₂

**Effective Treatment of Neurodegenerative Diseases**

ICAPP inhibits insulin stimulated aPKC activity, β-secretase activity and Aβ peptide production in brain of normal mice

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