A Multi-Target Chronopharmacotherapy for the Inhibition and Clearance of Toxic Proteins in Alzheimer's Disease

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Purpose: About 7.2 million Americans are living with Alzheimer's Disease (AD), with the number expected to to double by 2060. Currently used drugs for AD only reduce disease symptoms and marginally improve cognitive and memory functions. The purpose of this investigation is to develop a therapy for the inhibition and clearance of beta amyloid plaques in AD. Hypothesis: It's hypothesized that the combination of amyloid plaque degradation agent (Neprilysin), with amyloid aggregation inhibitor (Proanthocyanidin), will increase amyloid plaque clearance in-vitro and in-vivo. Procedure: The effect of neprilysin and proanthocyanidin, alone, and in combination on the Amyloid Beta 1-42 and Amyloid Beta 1-40 formation at different time periods (1, 2 and 4 days), was tested in amyloidogenic neural cultures. Amyloid Beta 1-42 and Amyloid Beta 1-40 concentration in the supernatant of the neural cultures was tested by ELISA. In vivo efficacy of these agents was tested in amyloidogenic C. Elegans model (GMC 101). Toxicity of these agents was tested by observing the change in the morphology of the neural cultures. Results: Both neprilysin and proanthocyanidin showed significant reduction in the production of Amyloid Beta 1-42 and Amyloid Beta 1-40 in the amyloidogenic neural cultures as compared to the control (Two - Way ANOVA followed by Turkey's post hoc test, $p<0.05$). Both these agents reduced the production of amyloid proteins in C. Elegans with no significant toxicity as observed under the microscope. Conclusion: Neprilysin and proanthocyanidin, and their combination have shown remarkable efficacy in the amyloidogenic hiPSC cultures, and in C. elegans model. This combination strategy has high translational potential for AD prevention and treatment.

Awards Won:

Third Award of $1,200