Moving Towards the Cure: Investigating the Effect of cAMP-Dependent Molecular Mechanisms on the Regulation of MAPT Gene Expression and the Formation of Neurofibrillary Tangles to Identify Drug Targets for Alzheimer's Disease

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The purpose of this experiment was to identify molecular mechanisms involved with the regulation of the MAPT gene and the subsequent formation of neurofibrillary tangles in Alzheimer’s disease, for the purpose of developing new genetic treatments. The researcher hypothesized that if the MAPT gene is regulated by a cAMP response element, activated through a Protein Kinase A (PKA) dependent phosphorylation cascade, then PS199202 tau will be over-expressed and result in the formation of neurofibrillary tangles because cAMP elements associated with a PKA phosphorylation cascade are prominent in the formation of multiple neuropeptides, especially those with a role in neurodegenerative diseases.Using many processes, including the BCA protein assay and Western Blot, positive results were obtained. In ten trials, the levels of hyperphosphorylated tau and phosphorylated CREB protein were significantly higher than in the control. A dose-response curve was created by measuring the effects of six-different doses of cAMP. The curve showed a directly positive relationship between the strength of the dose and the amount of phosphorylated CREB and hyperphosphorylated tau. This supports the researcher’s hypothesis by showing increased levels of the CREB transcription factor led to increased levels of phosphorylated tau. A T-test showed statistical significance was extremely high between the control and experimental values within the CREB and phosphorylated tau samples. These results clearly demonstrate that CREB, when activated by a Protein Kinase A phosphorylation cascade, is responsible for the hyperphosphorylation of tau. If these results are supported through further experimentation, this research can provide novel drug targets for Alzheimer’s disease treatments.

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