Effect of Protein Kinase Inhibitors on Tau Hyperphosphorylation as a TBI Cell-Based Model

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Tauopathies, for example Alzheimer’s disease (AD), affect over 5.5 million Americans, and are estimated to affect 16 million people by 2050. Tauopathies are diseases caused by the damage of tau protein, which are essential neuronal proteins. Traumatic Brain Injuries (TBI), Chronic Traumatic Encephalopathy (CTE), and other tauopathies have been contributors to neurodegeneration. Brain injuries trigger a phosphorylation reaction with inhibitors, which phosphorylate tau proteins. When tau is hyperphosphorylated by inhibitors, the tau protein detaches, forms neurofibrillary tangles (NFTs) and attaches to senile plaques, which disrupt the synapses and functions of neurons. This process of neurodegeneration is the main causes of AD. To test the effects of different inhibitors, a hyperphosphorylation model was created. The inhibitors tested are found in our daily nutrition such as sugar alcohols, sugar substitutes, and other supplements, and are thought to be harmful in high concentrations. To test the effects of tauopathies and its correlation to the inhibitors, a N2A nueroblastoma mice cell line was treated with different inhibitor concentrations: Okadaic Acid (OA) (100 nM and 1 μM), Sorbitol (0.1 mM, 0.5 mM, 1 mM), Calyculin A (0.1 μM, 1.25 μM), and Cyclosporin A (100 μM). The cells were treated and measured for phosphorylated-tau concentrations through Western Blots. Specific antibodies (including CP13, DA9, PHF-1, Fodrin, and ß-actin). OA created the most phosphorylation, followed by Sorbitol and Calyculin. Key Words: Traumatic Brain Injuries (TBI), Alzheimer’s Disease (AD), Microtubule associated proteins (MAP), Pair helical filaments (PHF), Phosphorylated Tau (p-tau), Neurofibrillary Tangles (NFT), Sorbitol, Okadaic Acid (OA), Calyculin A, Cyclosporin A

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