A Neuronal Cell Study Probing Tau Hyperphosphorylation as a Model for Chronic Traumatic Encephalopathy (CTE)

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The tau protein is a microtubule associated protein that’s maintained mainly through phosphorylation. Phosphorylation is upheld through two enzymes; kinases and phosphatases. There can be an inhibition to phosphatases, causing tau to hyperphosphorylate, disassociate from microtubules, and form insoluble aggregates called neurofibrillary tangles. This is thought to play a role in chronic traumatic encephalopathy (CTE). There is no way to diagnose this disease in living people, and the need to model it and find kinase inhibitors for it is imminent. This experiment compared various conditions (phosphatase inhibitors, proteolysis inhibitors, incubation time and temperature) to see which combination optimized the maximum amount of tau hyperphosphorylation in a CTE N2a cell model, and then tested various kinase inhibitors (LiCl, K252 alpha, STS) to see which one restored normal phosphorylation levels the best. N2a cell treatments and western blots were conducted. Results showed that the treatment containing only okadaic acid was the most effective in probing tau hyperphosphorylation. The other conditions were observed, and it was found that okadaic acid containing ZD proteolysis inhibitor and treating cells for 6hrs at 37C further enhanced the model. Then using the best model for CTE, the kinase inhibitor test was conducted and it was found that STS did the best in reducing phosphorylation levels. This model could help test possible biomarkers or drugs for CTE in the most effective and efficient manner and supports STS as a possible future treatment. Furthermore, general awareness for CTE is crucial so its patients who exhibit aggressive behaviors are better understood.

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