

# Inhibition of tau phosphorylating protein kinase cdk5 prevents ?-amyloid-induced neuronal death

Alvarez, Alejandra

Toro, Rodrigo

Cáceres, Alfredo

Maccioni, Ricardo B.

The key target of this study was the tau protein kinase II system (TPK II) involving the catalytic subunit cdk5 and the regulatory component p35. TPK II is one of the tau phosphorylating systems in neuronal cells, thus regulating its functions in the cytoskeletal dynamics and the extension of neuronal processes. This research led to demonstration that the treatment of rat hippocampal cells in culture with fibrillary ?-amyloid (A?) results in a significant increase of the cdk5 enzymatic activity. Interestingly, the data also showed that the neurotoxic effect of 1-20 ?M A? on primary cultures markedly diminished with co-incubation of hippocampal cells with the amyloid fibers plus the cdk5 inhibitor butyrolactone I. This inhibitor protected brain cells against A?-induced cell death in a concentration dependent fashion. Moreover, death was also prevented by a cdk5 antisense probe, but not by an oligonucleotide with a random sequence. The cdk5 antisense also reduced neuronal expression of c