

Calcium/calmodulin-dependent protein kinase type IV Is a target gene of the Wnt/ β -catenin signaling pathway

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Calcium/calmodulin-dependent protein kinase IV (CaMKIV) plays a key role in the regulation of calcium-dependent gene expression. The expression of CaMKIV and the activation of CREB regulated genes are involved in memory and neuronal survival. We report here that: (a) a bioinformatic analysis of 15,476 promoters of the human genome predicted several Wnt target genes, being CaMKIV a very interesting candidate; (b) CaMKIV promoter contains TCF/LEF transcription motifs similar to those present in Wnt target genes; (c) biochemical studies indicate that lithium and the canonical ligand Wnt-3a induce CaMKIV mRNA and protein expression levels in rat hippocampal neurons as well as CaMKIV promoter activity; (d) treatment of hippocampal neurons with Wnt-3a increases the binding of β -catenin to the CaMKIV promoter; (e) In vivo activation of the Wnt signaling improve spatial memory impairment and restores the expression of CaMKIV in a mice double transgenic model for Alzheimer's disease which shows