

The protein kinase cdk5: Structural aspects, roles in neurogenesis and involvement in Alzheimer's pathology

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A set of different protein kinases have been involved in tau phosphorylations, including glycogen synthase kinase 3b (GSK3b), MARK kinase, MAP kinase, the cyclin-dependent kinase 5 (Cdk5) system and others. The latter system include the catalytic component Cdk5 and the regulatory proteins p35, p25 and p39. Cdk5 and its neuron-specific activator p35 are essential molecules for neuronal migration and for the laminar configuration of the cerebral cortex. Recent evidence that the Cdk5/p35 complex concentrates at the leading edge of axonal growth cones, together with the involvement of this system in the phosphorylation of neuronal microtubule-associated proteins (MAPs), provide further support to the role of this protein kinase in regulating axonal extension in developing brain neurons. Although the aminoacid sequence of p35 has little similarity with those of normal cyclins, studies have shown that its activation domain may adopt a conformation of the cyclin-folded structure. The computed