

CDK5: A Unique CDK and Its Multiple Roles in the Nervous System

Cortés, Nicole

Guzmán-Martínez, Leonardo

Andrade, Víctor

González, Andrea

Maccioni, Ricardo B.

The cyclin-dependent kinase 5 (CDK5) is known as an exceptional component of the CDK family, due to its characteristic regulatory pathways and its atypical roles in comparison to the classical cyclins. Despite its functional uniqueness, CDK5 shares a great part of its structural similarity with other members of the cyclin-dependent kinase family. After its discovery 26 years ago, a progressive set of cellular functions has been associated with this protein kinase, ranging from neuronal migration, axonal guidance, and synaptic plasticity in diverse stages of brain development, including specific and complex cognitive functions. More than 30 substrates for CDK5 have been found in different cellular pathways. Together with its essential physiological roles, a major discovery was the finding twenty years ago that CDK5 participates in neurodegenerative diseases responsible for tau hyperphosphorylations, and, as a consequence, it becomes a neurotoxic factor. This review focuses on the wide roles of CDK5 in the central nervous system, its implications in neurodegeneration, and provides an integrative insight of its involvement in pain modulation, Alzheimer's disease, and other contexts.