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## Title

### ***JNK signaling and its impact on neural cell maturation and differentiation***

## Abstract

C-Jun-N-terminal-kinases (JNKs), members of the mitogen-activated-protein-kinase family, are significantly linked with neurological and neurodegenerative pathologies and cancer progression. However, JNKs serve key roles under physiological conditions, particularly within the central-nervous-system (CNS), where they are critical in governing neural proliferation and differentiation during both embryogenesis and adult stages. These processes control the development of CNS, avoiding neurodevelopment disorders. JNK are key to maintain the proper activity of neural-stem-cells (NSC) and neural-progenitors (NPC) that exist in adults, which keep the convenient brain plasticity and homeostasis. This review underscores how the interaction of JNK with upstream and downstream molecules acts as a regulatory mechanism to manage the self-renewal capacity and differentiation of NSC/NPC during CNS development and in adult neurogenic niches. Evidence suggests that JNK is reliant on non-canonical Wnt components, Fbw7-ubiquitin-ligase, and WDR62-scaffold-protein, regulating substrates such as transcription factors and cytoskeletal proteins. Therefore, understanding which pathways and molecules interact with JNK will bring knowledge on how JNK activation orchestrates neuronal processes that occur in CNS development and brain disorders. © 2024 The Authors

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adezmapimod; cyclin D1; cytoskeleton protein; diosgenin; gamma interferon; integrin; interleukin 1beta; interleukin 2; interleukin 4; interleukin 6; low density lipoprotein receptor related protein 6; mitogen activated protein kinase; mitogen activated protein kinase 1; mitogen activated protein kinase p38; nestin; nilotinib; Notch1 receptor; paxillin; protein p53; Rho guanine nucleotide binding protein; scaffold protein; stress activated protein kinase; toll like receptor 5; transcription factor; transcription factor Sox2; transforming growth factor beta; ubiquitin protein

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ligase; ubiquitin protein ligase E3; uvomorulin; adult; Alzheimer disease; apoptosis; astrocyte; attention deficit hyperactivity disorder; autism; binding affinity; blastocyst; brain disease; brain hemorrhage; brain ischemia; brain size; cancer growth; carcinogenesis; cell cycle progression; cell differentiation; cell fate; cell maturation; cell migration; cell proliferation; cell survival; central nervous system; cognition; developmental delay; electroporation; embryo development; female; gene expression; genetic transfection; hippocampus; homeostasis; image quality; induced pluripotent stem cell; JNK signaling; Macaca fascicularis; male; mass spectrometry; mesenchymal stem cell; microglia; morphogenesis; mouse; nerve cell; nerve cell differentiation; nerve cell plasticity; nerve fiber regeneration; nervous system development; nervous system inflammation; neural stem cell; neurite outgrowth; neuroepithelium cell; neurotoxicity; nonhuman; nuclear reprogramming; olfactory bulb; oocyte maturation; pericyte; pheochromocytoma; protein phosphorylation; rat; Review; signal transduction; somatic cell; spatial learning; subgranular zone; synaptogenesis; Wnt signaling

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