

JNK/SAPK PATHWAY

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Product Name	Cat #	Product Name	Cat #	Product Name	Cat #
ASK1, Active	M13-11G	MLK2, Active	M18-11G	SMAD3 Protein	S12-30G
BMP2K Protein	B03-11G	MLK3, Active	M19-11G	SMAD4 Protein	S13-30G
BMPR2, Active	B06-11H	MLK4, Active	M48-11G	SMAD5 Protein	S14-30G
c-JUN Protein	J05-55G	MST1, Active	S25-10G	SMAD9 Protein	S17-30G
DUSP22 (MKPX), Active	D22-20G	MST3, Active	S42-11G	STK3, Active	S24-10G
GCK, Active	M24-10G	MST4, Active	M59-10G	TAK1-TAB1, Active	M15-13G
GLK, Active	M25-11G	NFATC1 Protein	N12-30G	TAOK1, Active	T24-11G
HGK, Active	M26-11G	p53 Protein	P05-30BG	TAOK2, Active	T25-11G
HSF1 Protein	H25-30G	p53 Protein	P05-30G	TAOK3, Active	T26-11G
JNK1, Active	M33-10G	p63 Protein	P06-30G	TGFBR1 (ALK5), Active	T07-11G
JNK1, Unactive	M33-14G	p73 alpha Protein	P08-30G	TGFBR1, Unactive	T07-35G
JNK2, Active	M34-10BG	p73 beta Protein	P08-30BG	TGFBR2, Active	T08-11G
JNK2, Unactive	M34-14G	p73 gamma Protein	P08-30CG	TP53RK Protein	T29-34G
JNK3, Active	M35-10BG	RGS1 Protein	R39-30H	TRAF2 Protein	T57-30H
JNK3, Unactive	M35-14G	RIPK1 Protein	R07-34G	VAV1 Protein	V14-31G
MEKK1, Active	M09-11G	RIPK2, Active	R08-11G	VRK1, Active	V01-10G
MEKK2, Active	M10-10G	RIPK3, Active	R09-10G	VRK2, Active	V02-11G
MEKK3, Active	M11-10G	RIPK5, Active	R27-10G	VRK3 Protein	V03-30G
MEKK6, Active	M14-11G	SMAD1 Protein	S10-30G	ZAK, Active	Z01-10G
MLK1, Active	M17-11G	SMAD2 Protein	S11-30G		

JNK/SAPK Pathway

JNK/SAPK is a member of the MAPK family, which was originally identified as a stress-activated kinase linked to the death response (1). There are three isoforms of JNK/SAPK; these include: JNK1, JNK2, and JNK3. Activated JNK/SAPK can translocate to the nucleus where it can regulate the activity of multiple transcription factors including c-Jun, ATF-2, SMAD4, p53 and ELK1. More recently, JNK/SAPK has been shown to have additional cellular functions such as key role on cell growth, differentiation and survival.

JNK/SAPK is a central component in the JNK/SAPK signaling pathway. The pathway can be activated by various stimuli such as a variety of environment stresses, inflammatory cytokines, growth factors and GPCR agonists can activate this target and the pathway (2).

A variety of environmental stimuli impact the small GTPases of the Rho family (Rac, Rho and cdc42) in the cell membrane which, in turn lead to the activation of membrane proximal protein components such as MEKKs, ASK1, TAK1/TAB1 or MLK3. These protein kinases then phosphorylate and activate MKK4/7, which mediates the activation of the JNK/SAPK family members (3).

JNK/SAPK dysregulation, as a result of oxidative stress, plays an important role in the increased phosphorylation of cytoskeletal proteins found in Alzheimer's disease (AD) (4). In hippocampal and cortical regions of individuals with severe AD, activated phospho-JNK/SAPK becomes localized exclusively in association with neurofibrillar alterations including neurofibrillary tangles, senile plaque neurites, neuropil threads and granulovacuolar degeneration structures, completely overlapping with tau-positive neurofibrillary pathology.

Therefore, targeting the JNK/SAPK signaling pathway may offer an effective therapy for pathological conditions of the central nervous system (CNS) (5). Recent genetic evidence and emerging pharmacological data indicate that activated JNK could also be critical in causing diabetes, insulin resistance and obesity (6).

REFERENCES

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4. Zhu, X. et al: Activation and redistribution of c-Jun N-terminal kinase/stress activated protein kinase in degenerating neurons in Alzheimer's disease. *J Neurochem*. 2001 Jan;76(2):435-41.
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