

# p38 PATHWAY

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Product Name	Cat #	Product Name	Cat #	Product Name	Cat #
ASK1, Active	M13-11G	MAPKAPK3, Unactive	M41-14G	p38 gamma, Active	M37-10BG
ATF1 Protein	A09-54G	MAPKAPK5, Active	M42-10G	p38 gamma, Unactive	M37-14G
ATF2 Protein	A10-55G	MEKK1, Active	M09-11G	p53 Protein	P05-30BG
ATG13 Protein	A113-30G	MEKK2, Active	M10-10G	p53 Protein	P05-30G
BMP2K Protein	B03-11G	MEKK3, Active	M11-10G	p63 Protein	P06-30G
BMPR2, Active	B06-11H	MEKK6, Active	M14-11G	p73 alpha Protein	P08-30G
GCK, Active	M24-10G	MNK1, Active	M54-10G	p73 beta Protein	P08-30BG
HSP27 Protein	H30-54G	MNK2, Active	M55-10G	p73 gamma Protein	P08-30CG
IkBA Protein	I20-30G	MSK1, Active	R19-10G	RGS1 Protein	R39-30H
IkBA Protein	I20-31G	MSK2, Active	R18-10G	RIPK1 Protein	R07-34G
IkBB Protein	I21-30G	NFATC1 Protein	N12-30G	RIPK2, Active	R08-11G
IRAK1 Protein	I09-35G	NFKB2 Protein	N13-31G	RIPK3, Active	R09-10G
IRAK2, Active	I10-10BG	p38 alpha, Active	M39-10BG	RIPK5, Active	R27-10G
IRAK3 Protein	I11-34G	p38 alpha, Unactive	M39-14G	SOD2 Protein	S27-30G
IRAK4, Active	I12-10G	p38 alpha, Unactive	M39-14U	TAOK1, Active	T24-11G
KDR, Active	K01-11G	p38 alpha (K53A), Unactive	M39-16H	TAOK2, Active	T25-11G
MAPKAPK2, Active	M40-11G	p38 beta, Active	M36-10BG	TAOK3, Active	T26-11G
MAPKAPK2, Active	M40-11H	p38 beta, Unactive	M36-14G	Tau Protein Marker	T08-07N
MAPKAPK2, Unactive	M40-14G	p38 delta, Active	M38-10BG	Tau-316 Protein	T02-54N
MAPKAPK3, Active	M41-10G	p38 delta, Unactive	M38-14G	Tau-352 Protein	T03-54N

# p38 Pathway

p38 MAPK is a serine/threonine kinase which was originally isolated from lipopolysaccharide (LPS) stimulated monocytes. It is a member of the MAPK family and a central component in the p38 signaling pathway. The p38 signaling pathway is rapidly activated by topoisomerase II, histone deacetylase inhibitors, osmotic shock, microtubule disassembly and UV light. Thus, the p38 pathway was traditionally associated with the stress and immune responses, but more recently it has been shown to be involved in apoptosis and cell differentiation (1). The p38 pathway can also regulate cellular growth and cell cycle checkpoints in different ways, depending on the cell type and the stimulus (2).

Diverse stimuli activate the p38 signaling pathway by stimulating membrane proximal components such as MEKKs, ASK1, TAK1/TAB1 or MLK3, which in turn phosphorylate and activate MKK3/6 and MKK4. The MKK3/6 and MKK4 are termed the p38 MAPK kinases and they mediate the activation of the p38 MAPK family members (3). p38 MAPK is involved in the regulation of HSP27, MAPKAPK2, MAPKAPK3, MNK1/2 and a variety of transcription factors including ATF-2, STAT1, MEF2 and ELK1.

p38 MAPKs represents a point of convergence for multiple signaling processes that are activated in inflammation and thus a key potential target for the modulation of cytokine production. Specific inhibitors of p38 MAPK block production of the major inflammatory cytokines (i.e. TNF $\alpha$  and IL-1) and other proteins (e.g. COX-2), and have been demonstrated to have anti-inflammatory properties in animal models of disease (4). A major function of the p38 MAPK pathway is post-transcriptional control of inflammatory gene expression.

Recent studies have shown cytokines are suppressed in humans following oral administration of p38 MAPK inhibitors. These results, in addition to proof of concept studies in rheumatoid patients, have established p38 MAPK inhibition as an avenue for the future management of pro-inflammatory cytokine based diseases (5). At present, at least seventeen p38 MAPK inhibitors have successfully advanced into clinical testing (6).

## REFERENCES

1. Zarubin, T. et al: Activation and signaling of the p38 MAP kinase pathway. *Cell Res.* 2005 Jan;15(1):11-8.
2. Pearce, A. K. et al: Integrating stress-response and cell-cycle checkpoint pathways. *Trends Cell Biol.* 2001 Oct;11(10):426-33.
3. Wang, W. et al: Sequential activation of the MEK-extracellular signal-regulated kinase and MKK3/6-p38 mitogen-activated protein kinase pathways mediates oncogenic ras-induced premature senescence. *Mol Cell Biol.* 2002 May;22(10):3389-403.
4. Saklatvala, J.: The p38 MAP kinase pathway as a therapeutic target in inflammatory disease. *Curr Opin Pharmacol.* 2004 Aug;4(4):372-7.
5. Westra, J. et al: p38 mitogen-activated protein kinase (MAPK) in rheumatoid arthritis. *Mini Rev Med Chem.* 2006 Aug;6(8):867-74.
6. Lee, M. R. et al: MAP kinase p38 inhibitors: Clinical results and an intimate look at their interactions with p38 $\alpha$  protein. *Curr Med Chem.* 2005;12(25):2979-94.

Product Name	Cat #
Tau-381 Protein	T04-54N
Tau-383 Protein	T05-54N
Tau-410 Protein	T06-54N
Tau-412 Protein	T07-54N
Tau-441 Protein	T08-54N
Tau-441 (1-391) Protein	T08-55CN
Tau-441 (1-421) Protein	T08-55BN
Tau-441 (50-391) Protein	T08-55ON
Tau-441 (50-421) Protein	T08-55NN
Tau-441 (50-441) Protein	T08-55MN
Tau-441 (99-441) Protein	T08-55JN
Tau-441 (127-421) Protein	T08-55KN
Tau-441 (151-391) Protein	T08-55FN
Tau-441 (151-421) Protein	T08-55EN
Tau-441 (151-441) Protein	T08-55DN
Tau-441 (216-391) Protein	T08-55LN
Tau-441 (231-391) Protein	T08-55IN
Tau-441 (231-421) Protein	T08-55HN

Product Name	Cat #
Tau-441 (231-441) Protein	T08-55GN
Tau-441 (244-372) Protein	T08-55N
Tau-441 (S198A) Protein	T08-53BN
Tau-441 (S198E) Protein	T08-53N
Tau-441 (S199E) Protein	T08-53CN
Tau-441 (S214A) Protein	T08-53DN
Tau-441 (K257T) Protein	T08-56N
Tau-441 (L266V) Protein	T08-56CN
Tau-441 (G272V) Protein	T08-56DN
Tau-441 (N279K) Protein	T08-56EN
Tau-441 (dK280) Protein	T08-52N
Tau-441 (dN296) Protein	T08-52BN
Tau-441 (P301L) Protein	T08-56FN
Tau-441 (P301S) Protein	T08-56GN
Tau-441 (S305N) Protein	T08-56HN
Tau-441 (V337M) Protein	T08-56JN
Tau-441 (S352L) Protein	T08-56KN
Tau-441 (S404A) Protein	T08-53HN

Product Name	Cat #
Tau-441 (S404E) Protein	T08-53GN
Tau-441 (R406W) Protein	T08-56MN
Tau-441, BRSK1-phosphorylated	T08-50N
Tau-441, BRSK2-phosphorylated	T08-50BN
Tau-441, CAMK2-phosphorylated	T08-50CN
Tau-441, GSK3beta-phosphorylated	T08-50FN
Tau-441, PHKG2-phosphorylated	T08-50KN
Tau-441, PKA-phosphorylated	T08-50LN
Tau-441, TTBK1-phosphorylated	T08-50ON
TP53RK Protein	T29-34G
TTBK1, Active	T17-11G
TTBK2, Active	T18-11G
VAV1 Protein	V14-31G
VRK1, Active	V01-10G
VRK2, Active	V02-11G
VRK3 Protein	V03-30G
ZAK, Active	Z01-10G