

MAPK/ERK PATHWAY

Product Name	Cat #	Product Name	Cat #	Product Name	Cat #
14-3-3 alpha/beta Protein	Y71-30G	ERK2, Unactive	M28-14U	KAT5 (TIP60), Active	K314-380G
14-3-3 alpha/beta Protein	Y71-30N	ERK5, Active	M32-10G	KAT6B (MYST4), Active	K315-381BG
14-3-3 epsilon Protein	Y75-30G	FAK, Active	P91-10G	KAT7 (MYST2), Active	K316-380G
14-3-3 epsilon Protein	Y75-30N	FAK, Active	P91-11H	KAT8 (MYST1) Protein	K317-31G
14-3-3 sigma Protein	Y86-30G	FGFR1 (FLT2), Active	F04-11G	KAT9 (ELP3) Protein	K318-30G
14-3-3 sigma Protein	Y86-30N	FGFR1 Mutant (V561M), Active	F04-13G	KDR, Active	K01-11G
14-3-3 theta Protein	Y84-30G	FGFR2, Active	F05-11G	KSR1, Active	K07-11G
14-3-3 theta Protein	Y84-30N	FGFR2 Mutant (K526E), Active	F05-12BG	KSR2, Active	K08-11G
14-3-3 zeta Protein	Y92-30G	FGFR2 Mutant (N549H), Active	F05-12G	KSR2 Mutant (R676S), Active	K08-12BG
14-3-3 zeta Protein	Y92-30N	FGFR2 Mutant (E565G), Active	F05-12CG	MBP Protein	M42-51N
ACK, Active	A05-11G	FGFR2 Mutant (K641R), Active	F05-12DG	MBP Protein	M42-54G
BMP2K Protein	B03-11G	FGFR2 Mutant (K659N), Active	F05-12EG	MEK1, Active	M02-10G
BMPR2, Active	B06-11H	FGFR3, Active	F06-11G	MEK1 (EE), Active	M02-12G
BRAF, Active	B08-11G	FGFR3 Mutant (K650E), Active	F06-12CG	MEK1, Unactive	M02-14BG
BRAF Mutant (V599E), Active	B08-13G	FGFR3 Mutant (K650M), Active	F06-12DG	MEK1, Unactive	M02-14H
Calmodulin 1 Protein	C01-30H	FGFR3 Mutant (K650Q), Active	F06-12EG	MEK1 (K97A), Unactive	M02-16H
CAMK1 beta, Active	C08-10G	FGFR3 Mutant (G697C), Active	F06-12FG	MEK2, Active	M03-10G
CAMK1 delta, Active	C09-10G	FGFR4, Active	F07-11G	MEK2, Unactive	M03-14G
CAMK1 gamma, Active	C10-10BG	FGFR4 Mutant (N535K), Active	F07-12G	MEKK1, Active	M09-11G
CAMK1 gamma, Active	C10-11G	FGFR4 Mutant (V550E), Active	F07-12BG	MEKK2, Active	M10-10G
CAMK1, Active	C07-10G	FGFR4 Mutant (V550L), Active	F07-12CG	MEKK3, Active	M11-10G
CAMK2 alpha, Active	C11-10G	FGFR4 Mutant (V550M), Active	F07-12DG	MEKK6, Active	M14-11G
CAMK2 beta, Active	C12-10H	FGFR, Active	F10-10G	MELK, Active	M50-11G
CAMK2 delta, Active	C13-10G	FLT1, Active	F11-11G	MNK1, Active	M54-10G
CAMK2 gamma, Active	C14-10G	FLT3, Active	F12-11G	MNK2, Active	M55-10G
CAMK4, Active	C15-10G	FLT3 Mutant (D835Y), Active	F12-12BG	NIK, Active	M22-11G
CAMKK1, Active	C17-10G	FLT4, Active	F13-11G	P300 Protein	P07-31G
CAMKK1, Active	C17-18G	FOS Protein	F66-30G	PAK1, Active	P02-10BG
CAMKK2, Active	C18-10G	FRS3 Protein	F80-30G	PAK1/CDC42, Active	P02-10G
CaMKPase Protein	P06-34G	FYN A, Active	F15-10G	PAK1, Unactive	P02-14G
CASK, Active	C19-11G	FYN C, Unactive	F15-14G	PAK1, Unactive	P02-17G
CBP Protein	C07-31G	GAB1 Protein	G03-30H	PAK2 Protein	P03-34G
CDC42 Protein	C08-30G	GRB2 Protein	G45-30G	PAK3, Active	P04-10G
COT, Active	M16-11G	GRB7 Protein	G45-30GG	PAK4, Active	P05-10BG
COT, Unactive	M16-15G	GRK1, Active	R03-10G	PAK6, Active	P06-10G
CREB1 Protein	C49-55G	GRK2, Active	A14-10G	PAK7, Active	P07-10G
DAPK1, Active	D01-11G	GRK3, Active	A15-11G	PASK, Active	P08-11G
DAPK2, Active	D02-10G	GRK5, Active	G03-10G	PCNA Protein	P11-30H
DAPK3, Active	D03-10G	GRK6, Active	G04-10G	PDGFR alpha, Active	P12-11G
DCAMKL1, Active	D14-10G	GRK7, Active	G05-10G	PDGFR alpha, Active	P12-18G
DCAMKL2, Active	D15-11G	HER2, Active	E27-11G	PDGFR alpha Mutant (T674I), Active	P12-12CG
DLK Protein	M20-31G	HER4, Active	E29-11G	PDGFR alpha Mutant (D842V), Active	P12-12BG
EGFR, Active	E10-11G	Histone H1 Protein	H10-54N	PDGFR beta, Active	P13-11G
EGFR Mutant (T790M), Active	E10-12EG	Histone H3 Protein	H12-54N	PEAK1, Active	P18-11G
EGFR Mutant (T790M L858R), Active	E10-12DG	ICK, Active	I01-10G	PEAK1, Unactive	P18-14G
EGFR Mutant (L858R), Active	E10-12BG	IGF1R, Active	I02-11H	PKAc alpha, Active	P51-10G
EGFR Mutant (L861Q), Active	E10-12CG	InsR, Active	I08-11G	PKAc beta, Active	P52-10G
EIF4E Protein	E34-30G	IRR, Active	I07-11G	PKAc gamma, Active	P53-10G
ELK1 Protein	E64-30G	IRS1 (N-Term) Protein	I40-35G	PKC alpha, Active	P61-10G
ERK1, Active	M29-10G	IRS1 (C-Term) Protein	I40-31G	PKC alpha, Active	P61-18G
ERK1, Active	M29-10U	KAT2A (GCN5), Active	K311-381G	PKC beta I, Active	P62-10G
ERK1 (K71A) Protein	M29-16H	KAT2B (PCAF), Active	K311-381BG	PKC beta II, Active	P63-10G
ERK1, Unactive	M29-14G	KAT3A (CREBBP), Active	K312-381G	PKC delta, Active	P64-10G
ERK1, Unactive	M29-14U	KAT3A (CREBBP) Protein	K312-31G	PKC epsilon, Active	P65-10G
ERK2, Active	M28-10G	KAT3B (EP300) Protein	K312-31BG	PKC eta, Active	P67-10G
ERK2, Unactive	M28-14G	KAT4 Protein	K313-31G	PKC gamma, Active	P66-10G

MAPK/ERK Pathway

The ERK pathway incorporates multiple signaling proteins including RAS, c-Raf, MEK1/2, ERK1/2 (ERKs), RSK 1/2/3 and transcription factors such as ELK and ETS (1). The ERK family members are activated by phosphorylation on tyrosine and threonine residues in response to mitogens and other stimuli by the MAP/ERK kinases or MEKs (ERKs also have the capacity to activate via autophosphorylation).

ERKs respond to mitogenic signals by phosphorylating multiple down-stream components which include transcription factors, protein kinases, protein phosphatases, cytoskeletal elements, regulators of apoptosis and a variety of other signaling-related molecules (2). Many of these substrates are localized in the nucleus and participate in the regulation of transcription upon stimulation. Other substrates are found in the cytosol and organelles.

Transforming agents utilize the ERK/MAPK pathway in inducing cell proliferation. The ERK pathway is often up-regulated in many human tumors thus, they represent an attractive target for the development of anticancer drugs (3). For instance, activating mutations in either BRAF or N-Ras leads to the activation of the ERK/MAPK pathway in most cutaneous melanomas (4). Inhibition of the ERK/MAPK pathway results in the dephosphorylation of the proapoptotic BCL2 family members BAD and BIM which lead to caspase activation and, ultimately, the demise of melanoma cells through the induction of apoptosis.

Because of its multiple roles in the acquisition of a complex malignant phenotype, specific blockage of the ERK pathway is expected to result in not only an anti-proliferative effect but also in anti-metastatic and anti-angiogenic effects in tumor cells. Recently potent small-molecule inhibitors targeting the components of the ERK pathway have been developed, some of which have reached the clinical trial stage (5).

REFERENCES

1. Rubinfeld, H. et al: The ERK cascade: A prototype of MAPK signaling. *Mol Biotechnol.* 2005 Oct;31(2):151-74.
2. Yoon, S. et al: The extracellular signal-regulated kinase: Multiple substrates regulate diverse cellular functions. *Growth Factors.* 2006 Mar;24(1):21-44.
3. Reddy, K. B. et al: Role of MAP kinase in tumor progression and invasion. *Cancer Metastasis Rev.* 2003 Dec;22(4):395-403.
4. Panka, D. J. et al: Targeting the mitogen-activated protein kinase pathway in the treatment of malignant melanoma. *Clin Cancer Res.* 2006 Apr 1;12(7 Pt 2):2371s-2375s
5. Kohno, M. et al: Targeting the ERK signaling pathway in cancer therapy. *Ann Med.* 2006;38(3):200-11.

Product Name	Cat #
PKC iota, Active	P68-10G
PKC mu, Active	P72-10G
PKC nu, Active	P73-10G
PKC theta, Active	P74-10G
PKC zeta, Active	P75-10G
PKD2, Active	P76-10G
PKD2 Mutant (G848E), Active	P76-12BG
PKD2 Mutant (G870E), Active	P76-12CG
PKN2/PRK2, Active	P71-10G
PKN3/PRK3, Active	P69-10G
PP1A, Active	P13-20G
PP1B, Active	P14-20G
PP2Aalpha, Active	P16-20G
PP2Abeta Protein	P17-34G
PP2B Protein	P18-34G
PP2Calpha, Active	P02-20G
PP2Cgamma, Active	P07-20G
PRKAR1A Protein	P57-30H
PRKAR1B Protein	P59-30H
PRKX, Active	P81-10G
PRKY Protein	P82-35G
PSKH1 Protein	P89-34G
PTK7 Protein	P95-35G
PTK9 Protein	P97-34G
PTPN11 (SHP2), Active	P38-21G
PYK2, Active	P92-11H
RAC1 Protein	R03-30G
RAC2 Protein	R04-30H
RAC3 Protein	R02-30H

Product Name	Cat #
RAF1 (EE), Active	R01-13G
RAS Protein	R05-30G
RGS1 Protein	R39-30H
RHEB Protein	R42-30H
RhoA Protein	R44-30H
RhoC Protein	R44-30CH
RhoD Protein	R44-30DH
RSK1, Active	R15-10G
RSK2, Active	R17-10G
RSK2 Mutant (I416V), Active	R17-12BG
RSK2 Mutant (Y483C), Active	R17-12DG
RSK2 Mutant (L608F), Active	R17-12CG
RSK3, Active	R16-10G
SMAD1 Protein	S10-30G
SMAD2 Protein	S11-30G
SMAD3 Protein	S12-30G
SMAD4 Protein	S13-30G
SMAD5 Protein	S14-30G
SMAD9 Protein	S17-30G
SRC, Active	S19-10G
SRC, Active	S19-18G
SRMS, Active	S20-11G
STAT1 alpha Protein	S52-50G
STAT1 beta Protein	S52-54G
STAT2 Protein	S53-54G
STAT3 Protein	S54-54G
STAT3 Protein	S54-54H
STAT4 Protein	S55-54H
STAT5 Protein	S56-54H

Product Name	Cat #
STAT5B Protein	S56-54BG
STAT6 Protein	S57-30G
STK9 Protein	C46-31G
STK16 Protein	S31-34G
STK19, Active	S35-10G
STK21 (CIT), Active	C52-11G
STK31 Protein	S45-35G
STK32B (YANK2), Active	Y04-10G
STK32C (YANK3), Active	Y05-11G
STK33, Active	S46-10G
STK35 (CLIK1) Protein	S47-35G
STK36, Active	S48-11G
STK39 (STLK3), Active	S51-10H
STK40 (SHIK) Protein	S54-34G
TAK1-TAB1, Active	M15-13G
TGFB1	T831-40N
TGFB3	T833-40CN
TGFB1 (ALK5), Active	T07-11G
TGFB1, Unactive	T07-35G
TGFB2, Active	T08-11G
VAV1 Protein	V14-31G
VRK1, Active	V01-10G
VRK2, Active	V02-11G
VRK3 Protein	V03-30G
YES1, Active	Y01-10G
ZAK, Active	Z01-10G