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Gene Section
Mini Review

MAPK6 (mitogen-activated protein kinase 6)

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Identity

Other names: ERK3; PRKM6; p97MAPK

HGNC (Hugo): MAPK6

Location: 15q21.2

Local order: The MAPK6 gene is located between the genes LEO1 and BCL2L10 on chromosome 15.

DNA/RNA

Description

The MAPK6 gene spans 47.01 kb on the long arm of chromosome 15 and is transcribed in the centromere-to-telomere orientation. The gene is composed of 6 exons with the translation initiation codon located in exon 2. The first two exons are separated by a long intron of 26.45 kb.

Transcription

The MAPK6 transcribed mRNA has 4,186 bp. No splice variants have been reported.

Pseudogene

Database analysis reveals the presence of six MAPK6 pseudogenes localized on four different chromosomes: MAPK6PS1 (8q11.23), MAPK6PS2 (21q21.1), MAPK6PS3 (13q14.13), MAPK6PS4 (8q11.1), MAPK6PS5 (8q23.1) and MAPK6PS6 (10q11.23). All six loci contain intronless copies of MAPK6 and display the features of processed pseudogenes.

Protein

Description

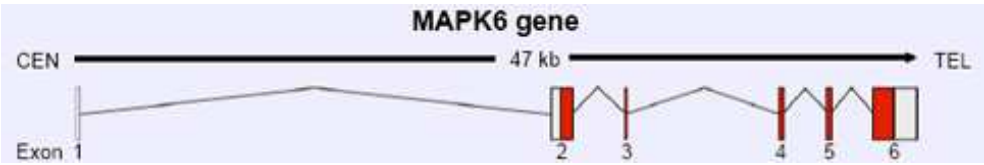
Extracellular signal-regulated kinase 3 (ERK3) is an atypical member of the mitogen-activated protein (MAP) kinase family of serine/threonine kinases. The human ERK3 protein is made of 721 amino acids and contains a typical kinase domain located at the N-terminal extremity. Another region with homology to the MAP kinase ERK4 (C34 domain) has been identified after the kinase domain. The function of the C34 domain is unknown.

Expression

MAPK6 mRNA is expressed ubiquitously. The highest levels of expression are observed in the skeletal muscle and brain. ERK3 is a highly unstable protein, with a half-life of less than one hour, that is constitutively degraded by the ubiquitin-proteasome pathway. Notably, oncogenic B-Raf signaling markedly up-regulates MAPK6 mRNA and protein levels.

Localisation

ERK3 localizes to the cytoplasm and nucleus of a variety of cultured cells.



Genomic organization of the MAPK6 gene on chromosome 15.

Schematic representation of the ERK3 protein structure. Kinase, catalytic kinase domain; C34 conserved region in ERK3 and ERK4; SEG, activation loop motif containing the regulatory phosphorylation residue Ser189.

Function

Little is known about the regulation and functions of ERK3. Overexpression of ERK3 in fibroblasts inhibits S-phase entry, suggesting that ERK3 may act as a negative regulator of cell proliferation in certain cellular contexts. The only known physiological substrate of ERK3 is the protein kinase MK5.

Homology

ERK3 display 73% amino acid identity with ERK4 in the kinase domain. ERK4 and ERK3 define a distinct subfamily of MAP kinases that is found exclusively in vertebrates.

Mutations

Note

No mutation reported yet.

Implicated in

Cancer

Note

DNA microarray studies have yielded conflicting data about the regulation of MAPK6 expression in cancer. Studies have shown that expression of MAPK6 mRNA is down-regulated in brain tumors, ovarian carcinoma and cutaneous melanoma, and up-regulated in leukemias, adrenocortical carcinoma, squamous cell lung carcinoma, salivary adenoid cystic carcinoma, tongue squamous cell carcinoma and cervical cancer. In prostate cancer, one study reported an inverse correlation between MAPK6 mRNA levels and the stage of the disease.

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