

## Gene Section

### Short Communication

# MAPK6 (mitogen-activated protein kinase 6)

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## Abstract

Review on MAPK6, with data on DNA, on the protein encoded, and where the gene is implicated.

### Keywords

MAPK4; ERK3; Kinase; signaling pathway; RAS-RAF-MAPK pathway

## Identity

HGNC (Hugo)

MAPK6

### Location

15q21.2

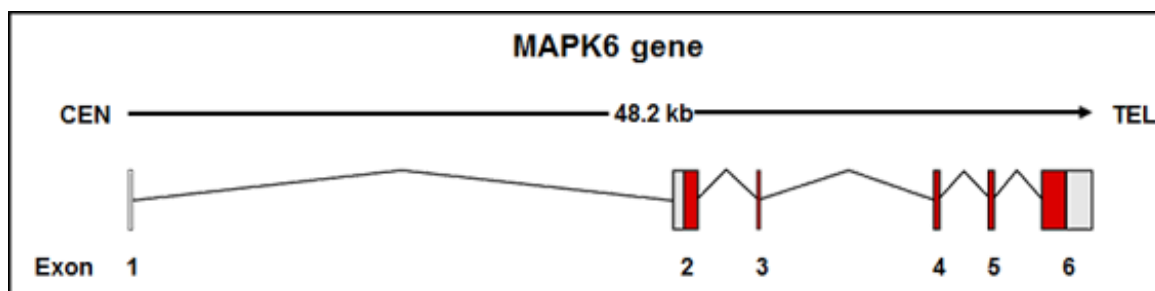
### Other names

ERK3, PRKM6, p97MAPK

### Local order

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

## DNA/RNA



Genomic organization of the MAPK6 gene on chromosome 15.

## 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.

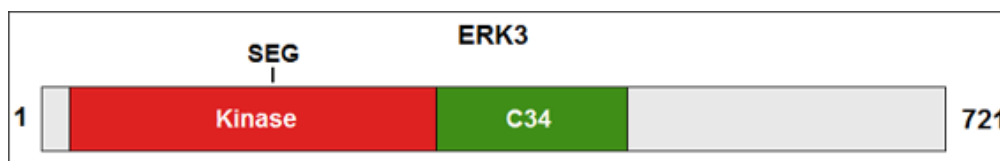
## Pseudogene

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



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.

### 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.

### Localisation

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

### Function

Little is known about the regulation and functions of ERK3. Recent studies suggest a potential involvement of the kinase in the control of cell differentiation, cytoskeletal remodelling, cell migration and invasion, DNA repair, and immune response. The best-characterized and validated substrate of ERK3 is the protein kinase MAPKAPK5 (MK5).

### Homology

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

## Mutations

No recurrent mutation in the MAPK6 gene has been reported in cancer.

## Implicated in

### Cancer

Studies have documented the upregulation of MAPK6 mRNA in squamous cell carcinomas of the skin, squamous cell lung carcinoma, and tongue

squamous cell carcinoma. Expression of MAPK6 mRNA is also increased in salivary adenoid cystic carcinoma, adrenocortical carcinoma, T-cell acute lymphoblastic leukemia, and acute myeloid leukemia. In lymphomas, reports have suggested an

increase of MAPK6 expression in Burkitt's lymphoma and a decrease in Hodgkin's lymphoma. Downregulation of MAPK6 mRNA level has also been observed in cutaneous melanoma, (colorectal adenocarcinoma and esophageal adenocarcinoma. The significance of these changes remains to be investigated.

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