

Gene Section

Short Communication

MAPK4 (mitogen-activated protein kinase 4)

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Published in Atlas Database: March 2017

Online updated version : <http://AtlasGeneticsOncology.org/Genes/MAPK4ID41293ch18q21.html>

Printable original version : <http://documents.irevues.inist.fr/bitstream/handle/2042/69006/03-2017-MAPK4ID41293ch18q21.pdf>
DOI: 10.4267/2042/69006

This article is an update of :

MAPK4 (mitogen-activated protein kinase 4). Atlas Genet Cytogenet Oncol Haematol 2017;21(12)

Meloche S. MAPK4 (mitogen-activated protein kinase 4). Atlas Genet Cytogenet Oncol Haematol 2009;13(1)

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Abstract

Review on MAPK4, with data on DNA, on the protein encoded, and where the gene is implicated.

Keywords

MAPK4; ERK4; Kinase; signaling pathway; RAS-RAF-MAPK pathway

Identity

HGNC (Hugo): MAPK4

Location: 18q21.1

Other names: ERK4, PRKM4, pP63mapk

Local order: The MAPK4 gene is located between the genes SKA1 (C18orf24) and MRO on chromosome 18

DNA/RNA

Description

The MAPK4 gene spans 171.7 kb on the long arm of chromosome 18 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 102.8 kb.

Transcription

The MAPK4 transcribed mRNA has 4,736 bp. No splice variants have been reported.

Pseudogene

None.

Protein

Description

Extracellular signal-regulated kinase 4 (ERK4) is an atypical member of the mitogen-activated protein (MAP) kinase family of serine/threonine kinases. The human ERK4 protein is made of 587 amino acids and contains a typical kinase domain located at the N-terminal extremity. Another region with homology to the MAP kinase ERK3 (C34 domain) has been identified after the kinase domain. The function of the C34 domain is unknown.

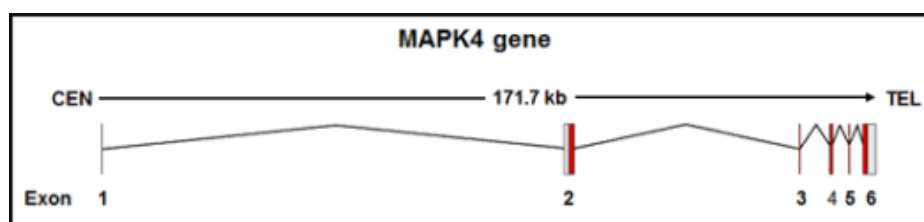


Figure 1. Genomic organization of the MAPK4 gene on chromosome 18.

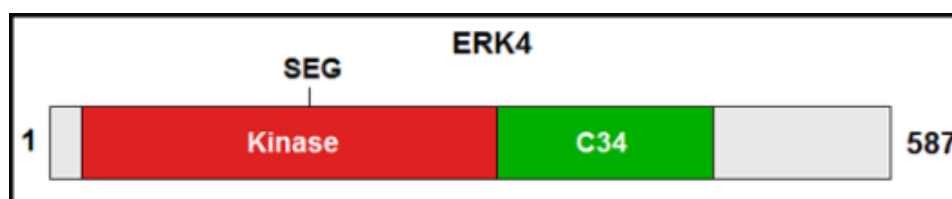


Figure 2. Schematic representation of the ERK4 protein structure. Kinase, catalytic kinase domain; C34 conserved region in ERK3 and ERK4; SEG, activation loop motif containing the regulatory phosphorylation residue Ser186.

Expression

MAPK4 mRNA is expressed to the highest level in the brain. Other sites of expression include the heart, lung, kidney, intestine, pancreas, parathyroid gland, prostate, thymus, ovary, eye and ear.

Localisation

ERK4 localizes to the cytoplasm and nucleus of a variety of cultured cells.

Function

Little is known about the regulation and functions of ERK4. The only known substrate of ERK4 is the protein kinase MAPKAPK5 (MK5).

Homology

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

Mutations

The R114C/H mutation has been reported in several types of cancer (colorectal adenocarcinoma, diffuse glioma, non-small cell lung cancer, cutaneous melanoma, stomach adenocarcinoma, uterine carcinosarcoma). The functional impact of this mutation on the expression or activity of ERK4 is not known.

Implicated in

Cancer

Analysis of copy number alterations (CNAs) from TCGA datasets show that MAPK4 gene is deleted in several adenocarcinomas, including prostate, esophageal, stomach and lung adenocarcinomas. Also, a chromosomal subregion containing the MAPK4 gene is deleted with high frequency (23%)

in pancreatic adenocarcinoma. On the other hand, MAPK4 is amplified with low frequency in neuroendocrine prostate cancer, diffuse large B-cell lymphoma and sarcomas.

Interrogation of the OncoPrint database reveals that expression of MAPK4 mRNA is downregulated in breast and prostate cancer.

Consistent with CNA analysis, MAPK4 mRNA is upregulated in diffuse large B-cell lymphoma.

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This article should be referenced as such:

Mathien S, Meloche S. MAPK4 (mitogen-activated protein kinase 4). *Atlas Genet Cytogenet Oncol Haematol.* 2017; 21(12):441-442.