

Gene Section

Short Communication

MAPK6 (mitogen-activated protein kinase 6)

Simon Mathien, Sylvain Meloche

Institute of Research in Immunology and Cancer, Université de Montréal, Montreal, Quebec H3C 3J7, Canada; simon.mathien@umontreal.ca; sylvain.meloche@umontreal.ca

Published in Atlas Database: March 2017

Online updated version : <http://AtlasGeneticsOncology.org/Genes/MAPK6ID43349ch15q21.html>

Printable original version : <http://documents.irevues.inist.fr/bitstream/handle/2042/68749/03-2017-MAPK6ID43349ch15q21.pdf>

DOI: 10.4267/2042/68749

This article is an update of :

Meloche S. MAPK6 (mitogen-activated protein kinase 6). *Atlas Genet Cytogenet Oncol Haematol* 2009;13(7)

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2018 *Atlas of Genetics and Cytogenetics in Oncology and Haematology*

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

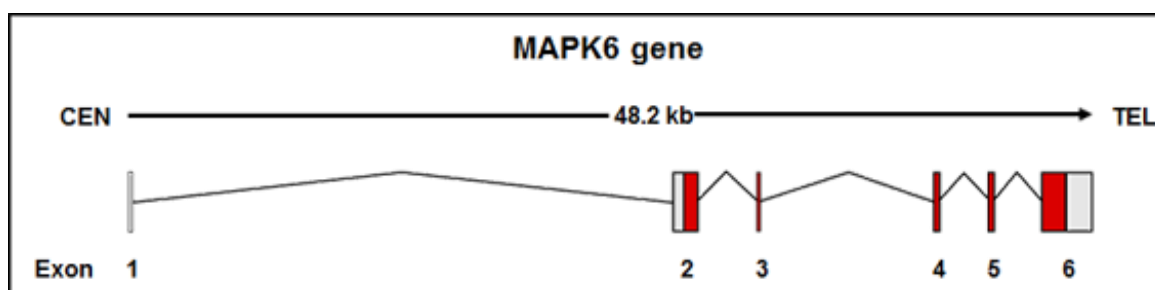
Other names

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.

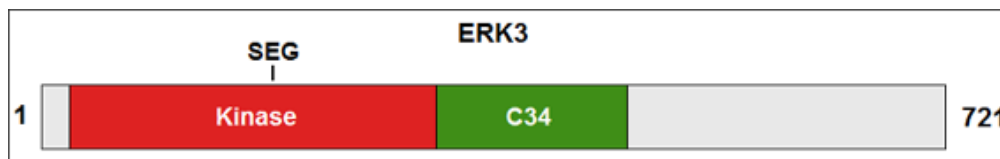
Pseudogene

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.

References

- Boulton TG, Nye SH, Robbins DJ, Ip NY, Radziejewska E, Morgenbesser SD, DePinho RA, Panayotatos N, Cobb MH, Yancopoulos GD. ERKs: a family of protein-serine/threonine kinases that are activated and tyrosine phosphorylated in response to insulin and NGF. *Cell*. 1991 May 17;65(4):663-75
- Brand F, Schumacher S, Kant S, Menon MB, Simon R, Turgeon B, Britsch S, Meloche S, Gaestel M, Kotlyarov A. The extracellular signal-regulated kinase 3 (mitogen-activated protein kinase 6 [MAPK6])-MAPK-activated protein kinase 5 signaling complex regulates septin function and dendrite morphology. *Mol Cell Biol*. 2012 Jul;32(13):2467-78
- Coulombe P, Meloche S. Atypical mitogen-activated protein kinases: structure, regulation and functions. *Biochim Biophys Acta*. 2007 Aug;1773(8):1376-87
- Crowe DL. Induction of p97MAPK expression regulates collagen mediated inhibition of proliferation and migration in human squamous cell carcinoma lines. *Int J Oncol*. 2004 May;24(5):1159-63
- Long W, Foulds CE, Qin J, Liu J, Ding C, Lonard DM, Solis LM, Wistuba II, Qin J, Tsai SY, Tsai MJ, O'Malley BW. ERK3 signals through SRC-3 coactivator to promote human lung cancer cell invasion. *J Clin Invest*. 2012 May;122(5):1869-80
- Marquis M, Daudelin JF, Boulet S, Sirois J, Crain K, Mathien S, Turgeon B, Rousseau J, Meloche S, Labrecque N. The catalytic activity of the mitogen-activated protein kinase extracellular signal-regulated kinase 3 is required to sustain CD4+ CD8+ thymocyte survival. *Mol Cell Biol*. 2014 Sep 15;34(18):3374-87
- Meloche S, Beatty BG, Pellerin J. Primary structure, expression and chromosomal locus of a human homolog of rat ERK3. *Oncogene*. 1996 Oct 3;13(7):1575-9

MAPK6 (mitogen-activated protein kinase 6)

Schumacher S, Laass K, Kant S, Shi Y, Visel A, Gruber AD, Kotlyarov A, Gaestel M. Scaffolding by ERK3 regulates MK5 in development. *EMBO J.* 2004 Dec 8;23(24):4770-9

Seternes OM, Mikalsen T, Johansen B, Michaelsen E, Armstrong CG, Morrice NA, Turgeon B, Meloche S, Moens U, Keyse SM. Activation of MK5/PRAK by the atypical MAP kinase ERK3 defines a novel signal transduction pathway. *EMBO J.* 2004 Dec 8;23(24):4780-91

Turgeon B, Lang BF, Meloche S. The protein kinase ERK3 is encoded by a single functional gene: genomic analysis of the ERK3 gene family. *Genomics.* 2002 Dec;80(6):673-80

Turgeon B, Saba-EI-Leil MK, Meloche S. Cloning and characterization of mouse extracellular-signal-regulated protein kinase 3 as a unique gene product of 100 kDa. *Biochem J.* 2000 Feb 15;346 Pt 1:169-75

Wang W, Bian K, Vallabhaneni S, Zhang B, Wu RC, O'Malley BW, Long W. ERK3 promotes endothelial cell functions by upregulating SRC-3/SP1-mediated VEGFR2 expression. *J Cell Physiol.* 2014 Oct;229(10):1529-37

Zhu AX, Zhao Y, Moller DE, Flier JS. Cloning and characterization of p97MAPK, a novel human homolog of rat ERK-3. *Mol Cell Biol.* 1994 Dec;14(12):8202-11

This article should be referenced as such:

Mathien S, Meloche S. MAPK6 (mitogen-activated protein kinase 6). *Atlas Genet Cytogenet Oncol Haematol.* 2018; 22(1): 5-7.
