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Gene Section
Mini Review

MAPK8 (mitogen-activated protein kinase 8)

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Identity

Other names: JNK1 (C-Jun N-terminal kinase 1); Stress-activated protein kinase 1 (SAPK1)

HGNC (Hugo): MAPK8

Location: 10q11.21

DNA/RNA

Description

The JNK1 gene maps on chromosome 10q11.21 spanning 130089 bp. It contains 22 confirmed introns, 20 of which are alternative.

Transcription

By alternative splicing, JNK1 gene encodes 13 different transcripts that translate to 13 JNK1 isoforms. The predicted molecular weight of JNK1 protein is 44.2 kD.

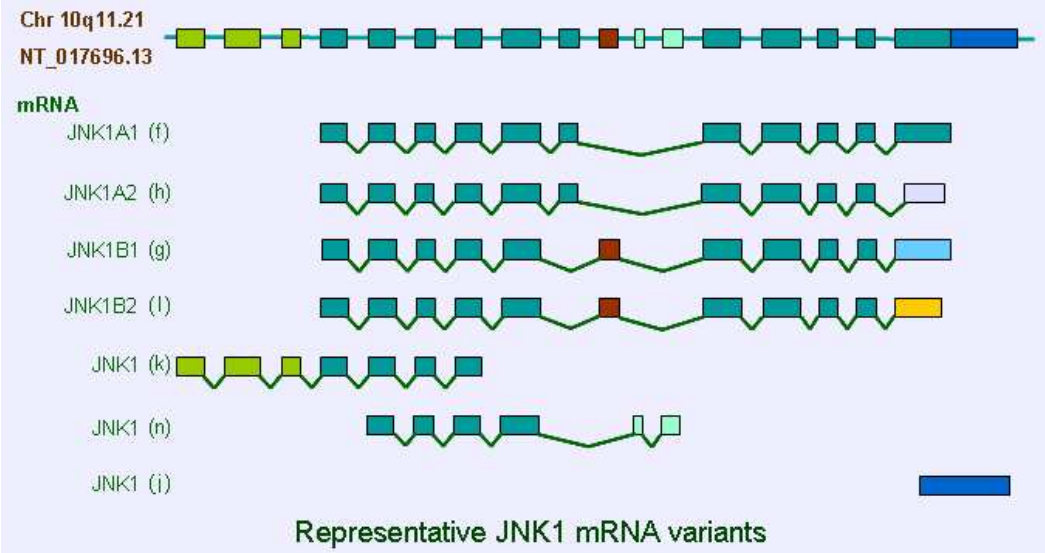
Protein

Description

All JNK proteins contain a protein kinase domain that belongs to a very extensive family of eukaryotic serine/threonine proteins kinase. A number of conserved regions have been identified in the catalytic domain of JNKs. In the N-terminal extremity of the catalytic domain there is a glycine-rich motif in the vicinity of a lysine residue, which has been shown to be involved in ATP binding. A conserved aspartic acid reside that is critical for the catalytic activity of kinase has also been identified in the central part of the catalytic domain.

Expression

JNK1 is ubiquitously expressed.



Representative JNK1 mRNA variants

Localisation

Cytoplasmic and nuclear.

Function

The members of JNK family act as an integration point for multiple intracellular biochemical signals governing a wide variety of cellular processes such as proliferation, differentiation, apoptosis, migration, transcriptional regulation, and development.

JNK targets specific transcription factors and thus mediates immediate-early gene expression in response to various stress signals including ultraviolet (UV) radiation, oxidative stress, protein malfolding in endoplasmic reticulum, osmotical shock, and inflammatory mediators. These transcription factors include AP-1, ATF-2, Elk-1, p53, etc... Several upstream dual specific protein kinases, such as MKK4/SEK1 and MKK7, can activate JNK through phosphorylation of the conversed Thr-Pro-Tyr motif on JNK proteins. In mammalian cells, activated JNK can phosphorylate the N-terminus of c-Jun, which contains both JNK docking site and JNK phosphorylation site (ser63 and ser73), orJunD, which lacks a JNK docking site but contains a JNK phosphorylation site. JNK is unable to phosphorylate JunB due to the lack of a JNK phosphorylation site inJunB, despite there is a functional JNK docking site. Comparison of the binding activity of JNK isoforms demonstrates that JNK2 bind c-Jun approximately 25 times more efficiently than did JNK1. Therefore, individual members of the JNK family may selectively target specific transcription factors in vivo.

One of the most important functions of JNK is the regulation of apoptosis. Emerging evidence indicates that JNK activation is obligatory for apoptosis induced by both receptor-mediated 'extrinsic' pathway or mitochondria-mediated 'intrinsic' pathway. JNK activation may contribute to the initiation of Fas-induced apoptosis, possibly through the amplification of autocrine or paracrine Fas signaling by JNK-dependent Fas ligand (FasL) gene expression. In addition, JNK has been indicated in the apoptosis induced by Daxx, a Fas death domain (FADD) interaction protein. Through its serine/threonine kinase activity, JNK may contribute to mitochondria-mediated apoptosis by phosphory-lating pro- or anti-apoptoticBcl-2 family proteins. Finally, JNK has also been indicated as an important kinase phosphorylating p53 and subsequently facilitating p53-dependent apoptotic responses.

Sustained JNK activation may be responsible for the enhanced apoptosis observed in RelA-/- or Ikkb-/- mouse embryonic fibroblasts treated with TNFa. It was suggested that deficiency of RelA or IKKb caused a decreased expression of XIAP or GADD45b, which may antagonize the activation of JNK activation. However, such speculation contradicts the previous observations indicating that both GADD45b and XIAP are activators, rather than inhibitors for JNK activation. Moreover, gene profiling in our recent studies indicated no substantial difference of basal or inducible GADD45b and XIAP mRNA in wild type cells and Ikkb-/- cells.

Implicated in

Obesity, insulin resistance, neurodegenerative diseases, inflammation, cancer

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