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Gene Section
Short Communication

EEF2K (eukaryotic elongation factor 2 kinase)

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Abstract

Eukaryotic elongation factor 2 kinase (eEF-2K) (also known as Calmodulin (CaM)-dependent elongation factor 2 kinase,CaMKIII) is an unusual calcium/calmodulin (Ca^{2+}/CaM)-dependent Threonin kinase that controls the rate of the elongation phase of protein synthesis through phosphorylating elongation factor 2 (eEF2) (Nairn et al., 1985; Ryazanov 1987; Mitsui et al., 1993; Redpath et al., 1993). Phosphorylation of eEF2 on Thr-56 disrupts the interaction between eEF-2 and the ribosome, leading to reduced protein synthesis. eEF-2K is regulated by phosphorylation by multiple signaling pathways and kinases at 11 different phosphorylation sides (Ryazanov et al., 1988; Carlberg et al., 1990; Abramczyk et al., 2011; Browne et al., 2004; Marshall et al., 2012; Chafouleas et al., 1981; Bowden et al., 2013). Hypoxia, nutrient deprivation and metabolic stress are all known to stimulate eEF-2K through activation of AMPK (Chafouleas et al., 1981).The activity of eEF-2K is increased in rapidly proliferating malignant cells and in cancer specimens, but is absent in normal adjacent tissues (Ashour et al., 2014b). eEF-2K promotes cell proliferation, invasion and tumorigenesis of some cancers. eEF-2K expression (mRNA) correlates with poor patient survival and prognosis (outcome) in some solid tumors, including breast , pancreatic cancer and glioblastoma (Meric-Bernstam et al., 2012). The activity of this kinase is increased in many cancers and may be a potential therapeutic target in some cancers.

Keywords: Elongation, protein translation, proliferation, invasion, prognosis, survival, cancer

Identity

Other names: CaMK-III, eEF-2K, HSU93850
HGNC (Hugo): EEF2K
Location: 16p12.2

DNA/RNA

Note
EEF2K gene encodes a Ca2+/calmodulin-dependent kinase known as eukaryotic elongation factor-2 kinase (EEF2K).

Description

The EEF2K gene is composed of 18 exons. It spans approximately 80.35 kb of genomic DNA.

Transcription

This gene encodes 5 transcripts and protein coding transcript (EEF2K-001) has 7388 bp length and this is composed of 725 aa residues. EEF2K-002 is a non sense mediated decay. Other three transcripts (EEF2K-003, -004, -005) do not give rise to proteins.

Pseudogene

No pseudogene reported.

Protein

Description

Human eukaryotic elongation factor-2 kinase is composed of 725 amino acids (105 KDa) alfa-kinase catalytic domain of this protein is located at the section of 76-356. Calmoduline (CaM) binding domain is located close to N-terminal and next to the catalytic domain. The function of the region located

N-terminal of the CaM-binding site is not well understood but removal of this segment leads to intrinsic autophosphorylation and activity; cause inhibitory effect on the EF2K activity. Contain 18 phosphorylation sites. Autophosphorylated at multiple residues, Thr-348 is the major site. Towards the C-terminal region, there are four predicted alfa-helical regions, and these resemble SEL-1-type repeats. The region lies between SEL-1 type repeats and the C-terminus contains higly reserved sequences. The extreme C terminus is known to be essential for the phosphorylation of eukaryotic elongation factor-2 (eEF2).

Expression

Ubiquitosly expressed in nomal tissues. Activity is increased in some tumors.

Localisation

Cytoplasmic.

Function

EEF2K protein belongs to alfa-kinases family of protein kinases. Its activity is dependent to Ca2+/calmodulin kinase and phosphorilates eukaryotic elongation factor-2 (eEF2) at Thr56 and inhibits it association/binding with ribosomes, thus regulates the elongation phase of translation.

Mutations

No mutations identified other than SNPs repsesenting normal variations (http://www.hgmd.cf.ac.uk/ac/gene.php?gene=EEF2K)

Implicated in

Breast Cancer

Note

eEF-2K protein expression promotes in breast cancer cell survival, invasion, migration and tumorigenesis (Tekedereli et al., 2012). eEF-2k highly expressed lines compared with normal non-tumorigenic breast epithelium and ist expression is associated with poor patient survival and prognosis (Meric-Bernstam et al., 2012).

Prognosis

Overexpression of eEF-2k is associated with shorter survival and poor prognosis (outcome) in Estrogen receptor (ER) positive (Tekedereli et al., 2012) and triple negative or ER (-) breast cancer patients (Ozpolat et al in press).

Pancreatic cancer

Note

eEF-2K protein is significantly overexpressed in pancreatic cancer cell lines and its inhibition lead to inhibition of cell proliferation, in invasion and migration and induces apoptosis (Ashour et al., 2014a; Ashour et al., 2014b).

Glioblastome multiforme (GBM)

Note

eEF-2K protects cells from nutrient deprivation and in conferring tumor cell adaptation to nutrient deprivation and metabolic stress by blocking translation elongation (Bowden et al., 2013).

Azheimer' disease (AD)

Note

Levels of p-eEF2K were found to be significantly increased, and total eEF2 significantly decreased in AD, when compared to controls in the brain tissue. levels of p-MTOR (Ser2481), and EIF4EBP1 (p-4E-BP1) (Thr70 and Ser65) dramatically increase in AD, and are positively significantly correlated with total tau and p-tau proteins.

Hypertension

Note

eEF2K protein increases in mesenteric artery from spontaneously hypertensive rats (SHR). eEF2K mediates TNF-a-induced vascular inflammation via ROS-dependent mechanism, which is at least partly responsible for the development of hypertension in SHR (Usui et al., 2013).

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