HNRNPK (heterogeneous nuclear ribonucleoprotein K)

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Identity

Other names: CSBP; FLJ41122; HNRPK; TUNP
HGNC (Hugo): HNRNPK
Location: 9q21.32

Note
The heterogeneous nuclear ribonucleoproteins (hnRNPs) are a family of proteins that play fundamental roles in a variety of biological processes including cellular signaling, telomere elongation, DNA repair and the regulation of expression at both the transcriptional and translational levels. Among these proteins hnRNPK (K protein) is one of the most extensively studied. The ribonucleoprotein K orthologs were described in yeasts, fruit fly and worm (Bomszyt et al., 2004).

DNA/RNA

Description
The hnRNPK gene contains 17 exons spanning 12572 bp.

Transcription
Three alternatively spliced human hnRNPK trans-cripts are known. Both variant 1 (2995 bp) and variant 2 (2960 bp) encode a 464aa long isoform A and the variant 3 (2935 bp) product is the 463aa isoform B. The amino acid sequence at the C-terminus of the isoform A differs from the isoform B as follows: 459-463aa: (A)ADVEGF --> (B)SGKFF.

Pseudogene
At least three hnRNPK human pseudogenes have been found and are deposited in the pseudogene.org database.

Protein

Description
The hnRNPK protein (65kDa) is structurally related to four other poly(C)-binding proteins (PCBP) which contain three K homology (KH) domains that enable RNA and DNA binding with a high affinity towards polycytosine tracts. The KH domain is about 70 amino acids in length and is found in a variety of proteins from archaea through higher eukaryotes. hnRNPK also carries a nuclear localisation signal (NLS) and a nuclear shuttling domain (KNS) together which allow it to trans-locate between the cytoplasm and nucleus. It also contains a segment called the K protein interactive (KI) region, located between the KH2 and KH3 domain, which has an intrinsically disordered structure. This domain is not found in the other

![hnRNPK structure. The rectangles represent K homology domains (KH1, 2, 3), the K interactive region (KI), the nuclear localization signal (NLS) and the nuclear shuttling domain (KNS).](image-url)
PCBP proteins and is responsible for many of the known hnRNPK protein-protein interactions (Bomsztyk et al., 2004).

**Expression**
K protein is an abundant factor.

**Localisation**
Predominantly in the nucleus and cytoplasm; also found in mitochondria and plasma membrane.

**Function**
The functions of hnRNPK are defined by its modular structure that allows it to interact with both nucleic acids and proteins. It has been suggested that hnRNPK serves as a docking platform that facilitates the interaction between the molecular partners involved in the processes that compose gene expression, such as transcription and translation regulation, mRNA processing and chromatin remodeling (Bomsztyk et al., 2004). With regard to the factors implicated in the process of tumorigenesis, hnRNPK acts as a transcription activator for the CT element in the human c-myc promoter (Michelotti et al., 1996), the BRCA1 promoter (Thakur et al., 2003) and the basal promoter of the Eukaryotic translation initiation factor 4E-eIF-4E (Lynch et al., 2005). In response to DNA damage, hnRNPK is transiently recruited to the promoters of p53-responsive genes (p21) where it acts as a cofactor of TP53 protein and is required for triggering transcriptional activation (Moumen et al., 2005). A recent study identified K protein as a regulator of androgen receptor (AR) expression levels; it represses AR expression and androgen-induced prostate cancer cell growth through translational regulation of AR mRNA (Mukhopadhyay et al., 2009). In a loss-of-function screening system based on intracellular expression of single domain antibodies, hnRNPK was found as a potential target for cell migration and metastasis of human cancerous cells (Inoue et al., 2007).

**Homology**
Shares homology with four other PCBP proteins which contain three KH domains.

**Mutations**
Note
No mutation of human hnRNPK gene has been reported.

**Implicated in**

**Esophageal cancer**
Note
Expression analysis. A proteomic study on 72 esophageal squamous cell carcinoma cases and adjacent normal tissues in 57 of these cases. The study revealed that tumors with nodal metastases had a higher amount of hnRNPK than those without lymph node metastases. The expression of K protein was up-regulated in esophageal cancer tissues compared with normal tissues (Hatakeyama et al., 2006).

**Colorectal cancer**
Note
Expression analysis. A study utilizing a proteomic approach to compare the protein expression of normal colon epithelium to colorectal cancer tissues. The overexpression and cytoplasmatic localization of hnRNPK correlated with advancement of colorectal cancer. In normal colon K protein was detected only in the nucleus whereas in tumour tissues the protein was observed both in the cytoplasm and the nucleus (Carpenter et al., 2006).

**Lung cancer**
Note
Expression analysis. An examination of the expression of K protein and other hnRNPK proteins.
in lung cancer cell lines and biopsies from 32 lung cancer by real time RT-PCR and immunohistochemistry. Nuclear expression of hnRNP K in H460 cells increased from non-confluent to confluent cultures. In confluent cells hnRNP K protein was also found in the cytoplasm. Up-regulation of hnRNP K was observed in 60% of the tumors examined with a higher expression in adenocarcinomas (79%) versus squamous cell carcinomas (33%). In these cases the localization of the protein was mostly nuclear, but half of the positive cases revealed also cytoplasmic staining (Pino et al., 2003).  

**Nasopharyngeal carcinoma**

**Note**
An Immunohistochemical examination of hnRNP K and thymidine phosphorylase (TP) expression in 121 nasopharyngeal carcinoma cases. An aberrant cytoplasmic localization of hnRNP K and its overexpression was associated with poor survival of NPC patients (Chen et al., 2008).

**References**

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