

## Gene Section

### Mini Review

# HNRNPK (heterogeneous nuclear ribonucleoprotein K)

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Published in Atlas Database: March 2009

Online updated version: <http://AtlasGeneticsOncology.org/Genes/HNRNPKID44314ch9q21.html>

DOI: 10.4267/2042/44684

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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 trans-lational levels. Among these proteins hnRNP K (K protein) is one of the most extensively studied. The ribonucleoprotein K orthologs were described in yeasts, fruit fly and worm (Bomsztyk et al., 2004).

## DNA/RNA

### Description

The hnRNP K gene contains 17 exons spanning 12572 bp.

### Transcription

Three alternatively spliced human hnRNP K transcripts 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 hnRNP K human pseudogenes have been found and are deposited in the pseudogene.org database.

## Protein

### Description

The hnRNP K 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. hnRNP K 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

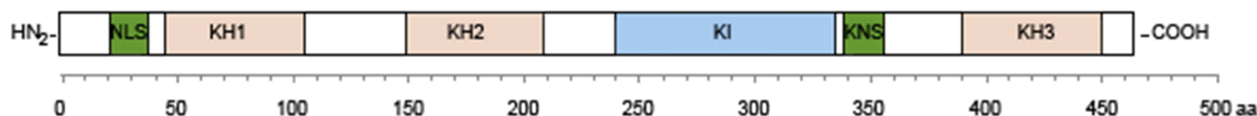


Fig.1 HNRNPK structure. The rectangles represent K homology domains (KH1, 2, 3), the K interactive region (KI), the nuclear localization signal (NLS) and the nuclear shuttling domain (KNS).

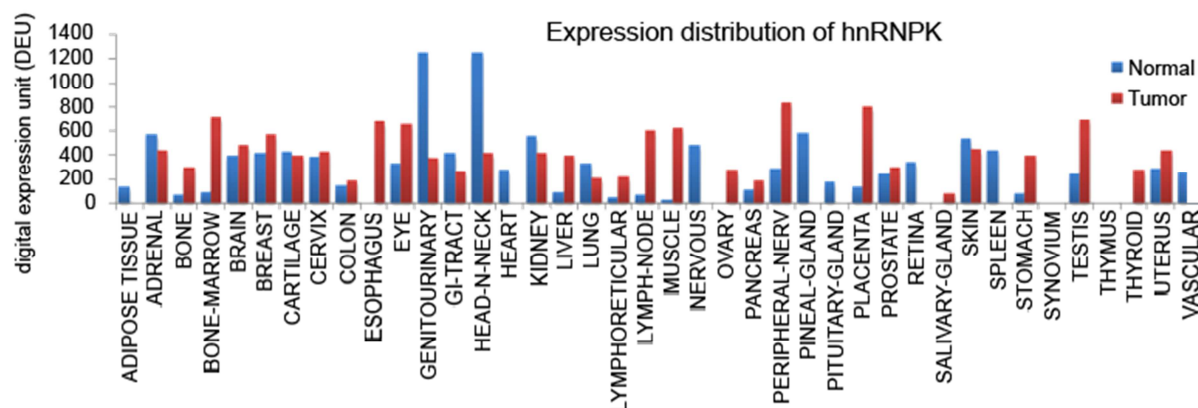


Fig.2 HnRNP K expression patterns in normal and cancer tissues based on human EST sequence abundance derived from the GeneHub-GEPIS database.

PCBP proteins and is responsible for many of the known hnRNP K protein-protein interactions (Bomszyk 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 hnRNP K are defined by its modular structure that allows it to interact with both nucleic acids and proteins. It has been suggested that hnRNP K 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 (Bomszyk et al., 2004). With regard to the factors implicated in the process of tumorigenesis, hnRNP K 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, hnRNP K 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, hnRNP K 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 hnRNP K 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 hnRNP K 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 cytoplasmic localization of hnRNP K 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 hnRNP 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).

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*This article should be referenced as such:*

Mikula M, Ostrowski J. HNRNPK (heterogeneous nuclear ribonucleoprotein K). *Atlas Genet Cytogenet Oncol Haematol.* 2010; 14(2):127-129.

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