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Gene Section
Mini Review

HTATIP2 (HIV-1 Tat interactive protein 2, 30kDa)

Jian Zhao

International Joint Cancer Institute, The Second Military Medical University, Shanghai, People's Republic of China (JZ)

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Identity

Other names: CC3; TIP30; SDR44U1; FLJ26963

HGNC (Hugo): HTATIP2

Location: 11p15.1

Note: HTATIP2, also called TIP30, is a transcriptional cofactor that enhances Tat-mediated transcription.

DNA/RNA

Description

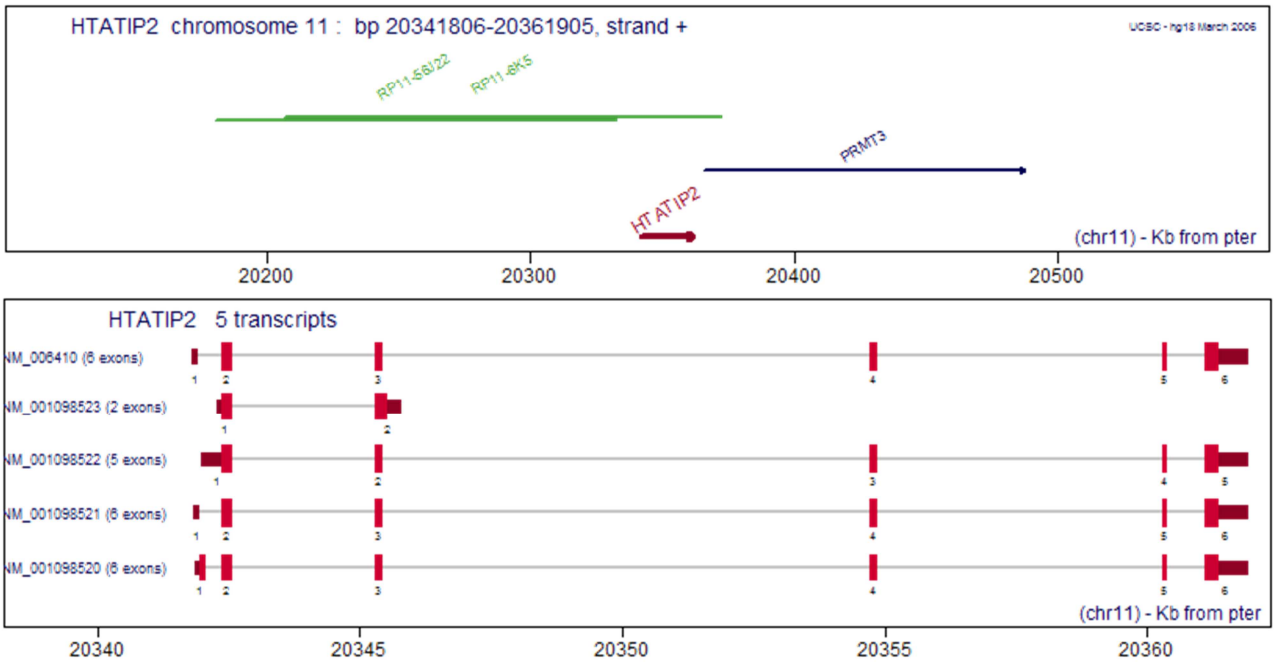
The human HTATIP2 gene has 6 exons that span more than 2.5 kb of genomic sequence located on chromosome 11p15.1.

Transcription

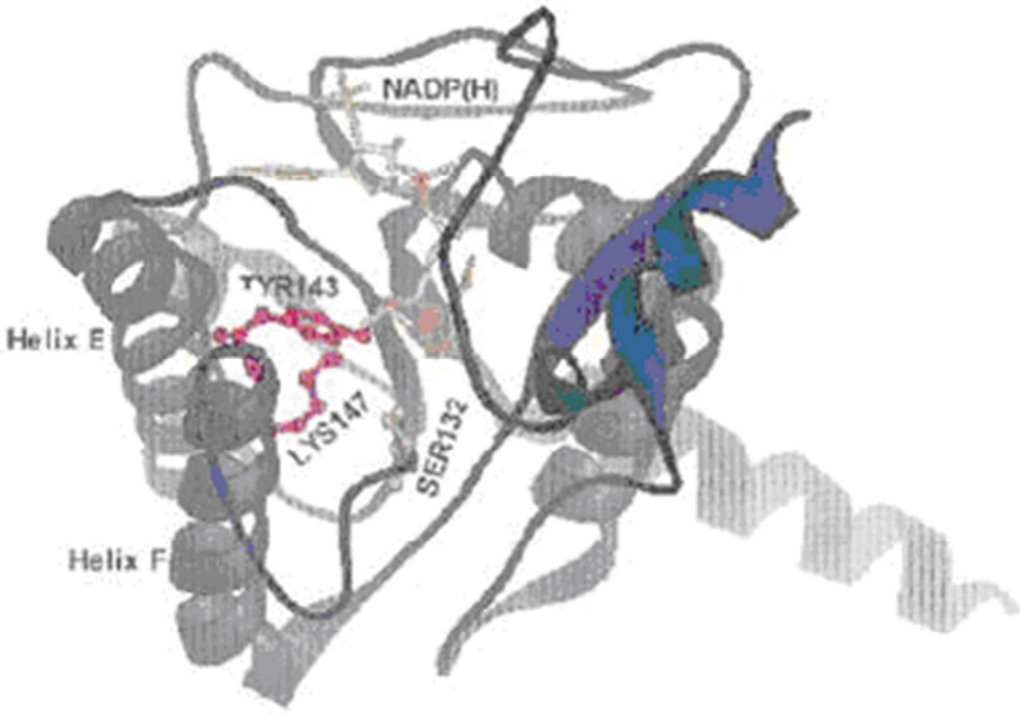
HTATIP2 has four types of transcripts with 1.5 kb, 1.4 kb, 1.7 kb and 1.4 kb and they encode the same protein, 242aa, as a result of alternative splicing. And a small type of HTATIP2 isoform is 0.78 kb composed of 2 exons coding a 133aa protein.

Pseudogene

None.



Genomic structure of published HTATIP2 alternatively spliced transcripts. Boxes indicate exons with coding regions in green. Red boxes indicate UTRs.



Structure model of HTATIP2/TIP30. Serine-132, tyrosine-143 and lysine-147, which correspond to the catalytically active residues in SDRs and NADPH are shown. The a-helices E and F normally involved in a dimer interface are labelled (Baker et al., 2000).

Protein

Description

HTATIP2 includes isoform a and isoform b, both of which contain 242aa, and isoform c, 131aa. HTATIP2 can interact with the N-terminal trans-activation domain of HIV-tat directly as 30kDa Tat-interacting protein, to activate the HIV-1 promoter (Xiao et al., 1998), and with an ERa-interacting coactivator CIA to repress the expression of c-myc (Jiang et al., 2004). It is a member of the short-chain dehydrogenases/reductases (SDR) family (Baker et al., 2000) and have a cavity of NADPH binding site in its structure (El Omari et al., 2005). HTATIP2 has Ser/Thr protein kinase activity, which can undergo autophosphorylation, and phosphorylates the heptapeptide repeats of the C-terminal domain of the largest RNA polymerase II subunit in a tat-dependent manner. HTATIP2 binds directly to the karyopherins of the importin beta family in a RanGTP-insensitive manner and associates with nucleoporins in vivo (King and Shtivelman, 2004).

Expression

HTATIP2 is an evolutionary conserved gene that is expressed ubiquitously in human tissues, while it is down-expressed in many tumors tissues, such as prostate, colon, liver, lung and breast cancers (Hewitt et al., 2000; Jiang et al., 2007; Lee et al., 2004; Varambally et al., 2002).

Localisation

HTATIP2 protein was found predominantly in the membrane and nuclear fractions but not in the particulate free cytoplasmic fraction (Whitman et al., 2000).

Function

The HTATIP2 gene is a tumor susceptibility gene, which is associated with the suppression of metastasis in small cell lung cancer (SCLC) (Shtivelman, 1997), hepatocarcinoma (Ito et al., 2003). HTATIP2 interacts with an Estrogen Receptor alpha-interacting coactivator CIA (coactivator independent of AF-2 function), to repress the expression of c-myc gene, and also associated with ets-1 to inhibit osteopontin transcription in human hepatocellular carcinoma (Zhao et al., 2008b). HTATIP2 forms a RanGTP-resistant complex with importins to inhibit nuclear import and induce apoptosis (King and Shtivelman, 2004). HTATIP2 also induces apoptosis under oxidative stress through stabilization of p53 mRNA (Zhao et al., 2008a).

Homology

HTATIP2 encodes a protein whose sequence is highly conserved in evolution, with homologous genes being present in Caenorhabditis elegans, Saccharomyces cerevisiae, Escherichia coli (Whitman et al., 2000), Branchiostoma belcheri (Wang et al., 2008), and Mus musculus.

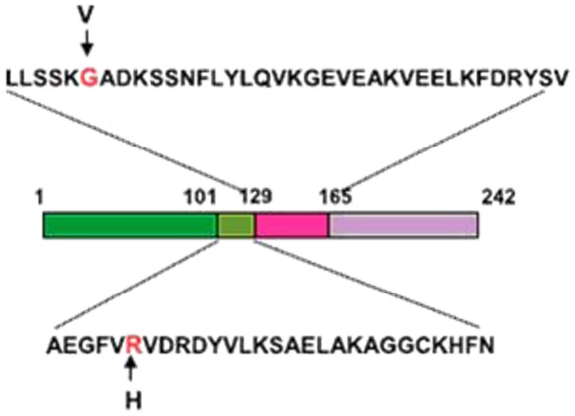
Mutations

Note

HTATIP2 mutant derived from hepatocellular carcinoma specimens promotes growth of HepG2 cells (Jiang et al., 2007).

Somatic

There are two types of HTATIP2 mutation, G134V and R106H, in hepatocellular carcinoma specimens (Jiang et al., 2007).



The red amino acids are mutated into other one, as schematic representation (Jiang et al., 2007).

Implicated in

Various carcinomas

Disease

HTATIP2 reported to be down-regulated in some kinds of cancers, such as lung cancer (NicAmhlaoibh and Shtivelman, 2001), hepato-cellular carcinoma (Zhao et al., 2008), gastric cancer (Li et al., 2009), prostate cancer (Zhang et al., 2008), breast carcinoma (Zhang et al., 2005; Zhao et al., 2007).

Multiple sclerosis (MS)

Disease

Oligodendrocyte precursor cells (OPCs) presist near the demyelinated axons arising in MS but inefficiently differentiate into oligodendrocytes and remyelinate these axons. Abnormal expression of HTATIP2, a direct inhibitor of Importin, is observed in these OPCs. Overexpression of HTATIP2 in a rat OPC cell line resulted in cytoplasmic entrapment of NICD and arrest of differentiation upon stimulation with Contactin- Fc.

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