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Gene Section
Mini Review

ELAVL1 (ELAV (embryonic lethal, abnormal vision, Drosophila)-like 1 (Hu antigen R))

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Identity

Other names: ELAV1; HUR; HuR; Hua; MelG

HGNC (Hugo): ELAVL1

Location: 19p13.2

DNA/RNA

Description

The ELAV1 gene, located on the minus strand, encompasses 47072 bp with 6 exons and 5 introns.

Transcription

mRNA of 2,3 kb but a second putative poly(A) signal is described leading to a 6 kb mRNA. Coding sequence from 168 to 1148 b.

Protein

Description

The HuR protein consists of 326 aa (36 kDa). HuR has three highly conserved motifs belonging to the RNA recognition motif (RRM) superfamily and a hinge region between RRMs 2 and 3 named the HuR nucleocytoplasmic shuttling (HNS) domain. It has been shown that the HNS domain regulates the localization of HuR by mediating its association with adaptor proteins for nuclear export such as pp32/PHAP-I and APRIL and with import factors transportin-1, transportin-2, and importin.

Expression

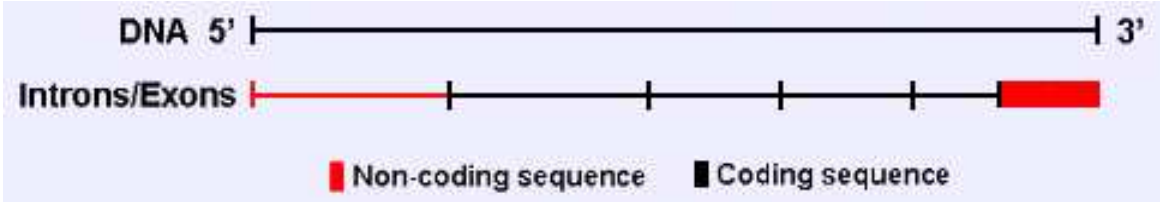
Ubiquitously expressed.

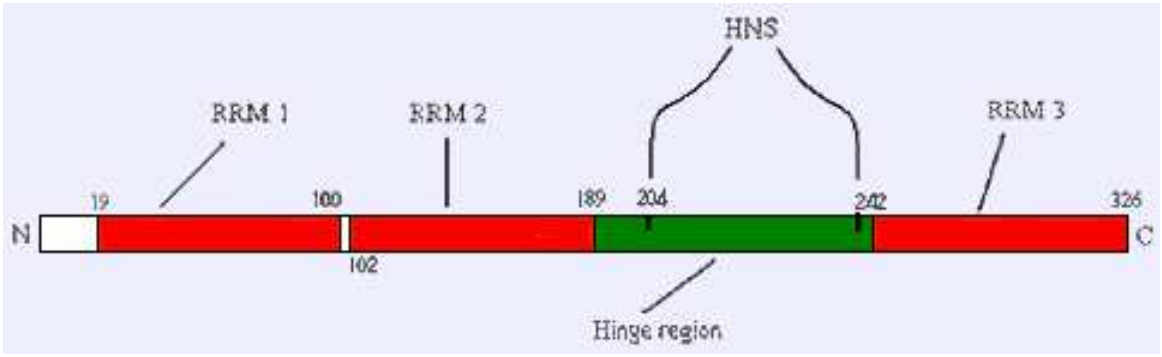
Localisation

Predominantly nuclear but shuttles between the nuclear and the cytoplasm.

Function

HuR belongs to the ELAV/Hu family (embryonic lethal abnormal vision phenotype in flies) of RNA-binding proteins (RBPs). Like other Hu/ELAVL RBPs, HuR contains 3 RRM through which it binds to specific mRNA and influences their post-transcriptional expression. HuR exhibits a high affinity for adenosine and uracil- (AU-) rich elements (ARE) leading to the stabilization and/or transport of its target host messages.





In addition to its role as an mRNA stabilizer and transporter, HuR has been shown to mediate the translation of mRNAs and rarely to repress translation. Moreover, HuR plays a key role in the enhancement of caspase-dependent apoptosis induced by extreme stress conditions. In response to a lethal stress, HuR accumulates in the cytoplasm, where it undergoes caspase-mediated cleavage. This cleavage appears to be important for pp32/PHAP-I - mediated enhancement of the caspase-dependent apoptosis. HuR was shown to play others critical functions in cells responding to immune stimuli, nutrient availability, and exposure to damaging agents. Similarly, it has an important regulatory function in the progression of cells through the division cycle, the implementation of differentiation programs, the promotion of cell migration, cell invasion and a malignant phenotype, and the inhibition of replicative senescence.

Mutations

Note

No HuR mutations have been found in cancer or other diseases.

Implicated in

Cancer

Oncogenesis

Breast, lung, colon and ovary cancer. Expression of HuR is increased in all cancer tissues compared to the normal-tissue counterparts. It exists a consistent correlation between HuR expression levels and advancing stages of malignancy.

Cachexia

Disease

Cachexia, characterized by the excessive loss of skeletal muscle, is frequently seen in patients with chronic diseases such as cancer. The bioactive gas nitric oxide has been identified as an important player in cancer-induced cachexia because NO is directly involved in the loss of MyoD mRNA (a key factor needed for the myogenic process, which is destabilized during cachexia) and muscle fiber. These events are mediated by the ability of HuR to associate and stabilize the message encoding the inducible NO synthase enzyme.

Hypertension

Disease

Chronic hypertension is associated with functional and morphological alterations of the vessel wall (ie, dysfunctional vascular endothelium and thickening of the smooth muscle layer). The pathomechanisms accounting for hypertension-induced vascular alterations are likely to be multifactorial. HuR is not only an important factor controlling vascular gene expression, but it is also subject to control by vasoactive factors that regulate cGMP and cAMP levels and downregulate its expression.

Paraneoplastic neurological disease

Disease

Paraneoplastic enecephalomyelitis/sensory neuronopathy (PEM/SSN) is characterized by the presence of a common autoantibody, referred to as anti-Hu or type I anti-neuronal nuclear antibody (ANNA-1). The target of these antibodies is the family of Hu antigens (Hel-N1, HuC, HuD and HuR).

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