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Gene Section
Mini Review

RBBP7 (retinoblastoma binding protein 7)

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Identity

Other names: RBAP46; RbAp46; RBBP-7; MGC138867; MGC138868

HGNC (Hugo): RBBP7

Location: Xp22.2

Note: RBBP7 is located at contig NP_002884.1 of GenBank. The retinoblastoma binding protein 7 gene symbol for human is RBBP7 whereas the symbol for the same gene for rat and mice is Rbbp7. RBBP7 was one of the two most abundant proteins from HeLa cell lysates that were specifically retained by an RB1 affinity column (Qian et al., 1993). Qian and Lee (1995) isolated cDNAs encoding RBBP7 by screening a HeLa cell cDNA expression library with monoclonal antibodies against RBBP7, which they called as RbAp46. Southern blot analysis indicated that the human genome contains a single copy of the RBBP7 gene.

DNA/RNA

Description

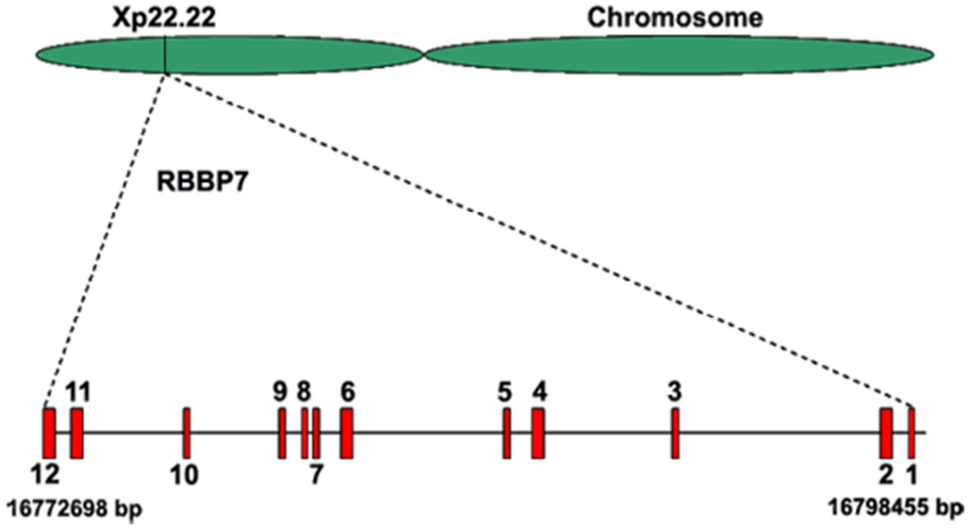
DNA size 27.75 kb; mRNA size 2021 bp; 12 exons.

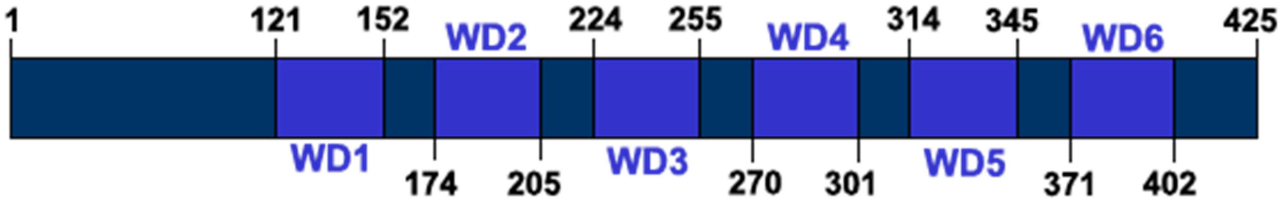
Protein

Description

425 amino acids; 47.82 kDa protein.

Post translational modifications: Phosphorylation enhances DNA binding. Phosphorylation occurs at position 95, 99, 354, 413 (Serine) and 416 (Threonine). Acetylation brings in a negative charge, acting to neutralise the positive charge on the histones and decreases the interaction of the N termini of histones with the negatively charged phosphate groups of DNA. As a consequence, the condensed chromatin is transformed into a more relaxed structure which is associated with greater levels of gene transcription.





The acetylation sites are: at 2 (Alanine), and 119 (Lysine).
Isoform: The following isoforms have been identified:
- RBBP7.iApr07
- hPA25320.1 (469 aa)
- hPA25320.2 (425 aa)
- hPA25320.3 (410 aa)
- hPA25320.7 (420 aa)

Expression

It is widely expressed.

Localisation

Nucleus.

Function

This protein is an ubiquitously expressed nuclear protein and it belongs to a highly conserved subfamily of WD-repeat proteins. It is found among several proteins that bind directly to retinoblastoma protein, which regulates cell proliferation. The encoded protein is found in many histone deacetylase complexes, including mSin3 co-repressor complex. It is also present in protein complexes involved in chromatin assembly, which include the type B histone acetyltransferase (HAT) complex, which is required for chromatin assembly following DNA replication; the core histone deacetylase (HDAC) complex, which promotes histone deacetylation and consequent transcriptional repression; the nucleosome remodeling and histone deacetylase complex (the NuRD complex), which promotes transcriptional repression by histone deacetylation and nucleosome remodelling. This protein can interact with BRCA1 tumor-suppressor gene and may have a role in the regulation of cell proliferation and differentiation.

Homology

The percent identity below represents identity of RBBP7 over an aligned region in UniGene.
- M. musculus : 100 (percentage identity)
- C. lupus familiaris : 100
- B. taurus : 100
- R. norvegicus : 100
- G.gallus : 96.2
- D. rerio : 94.4

Mutations

Note
Two types of mutation have been detected in the RBBP7 gene. A827G is a silent mutation and the other one is a missense type of mutation that changes N276S.

Implicated in

Breast cancer

Note
RBBP7 (also known as RbAp46) overexpression has shown to inhibit the tumorigenicity of neoplastigenic breast epithelial cells (Li et al., 2003). RBBP7 activates stress-induced apoptosis, the JNK-dependent apoptotic cell death, possibly through upregulation of GADD45 (Growth arrest- and DNA damage-inducible 45). GADD45 binds and activates MAPKKK MTK1/MEK4, the upstream regulator of JNK, triggering JNK-dependent apoptosis. Thus, overexpression of RBBP7 facilitates stress-induced apoptosis and suppresses tumorigenicity of neoplastigenic breast epithelial cells.

Leukemia

Note
Expression level of RBBP7 in initial acute leukemia has been found to be significantly higher than in chronic myelogenous leukemia. The Wilms tumor suppressor gene (WT1) expression level was also correlated with RBBP7 expression. WT1 encodes a zinc finger transcription factor that regulates transcription of its downstream gene. RBBP7 is a downstream effector of WT1 gene, and acts in a similar manner as WT1 does. It has been seen that high expression of RBBP7 suppresses the tumorigenicity of neoplastic breast epithelial cells but its overexpression possibly may induce leukemia. This phenomenon suggests that the regulatory pathway for RbAp46 gene expression in acute leukemia may be different from that in solid tumor.

Human embryonic kidney (HEK) 293 cell tumorigenesis

Note
High levels of RbAp46 suppress the tumorigenicity of adenovirus-transformed human embryonic kidney 293 cells. High level of RbAp46 resulted in G2/M cell population and augmented apoptosis in serum starved cells. It is possible that overexpression of RbAp46 may interfere with normal cell cycle and/or enhance apoptotic cell death which inhibits the transformation of tumor cells.

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