

Gene Section

Mini Review

RBBP8 (retinoblastoma binding protein 8)

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Identity

Other names: CTIP; RIM

HGNC (Hugo): RBBP8

Location: 18q11.2

DNA/RNA

Description

The gene encompasses 93.155 Kb of DNA.

Transcription

3279 bp mRNA.

Protein

Description

897 a.a. polypeptide.

Expression

Widely expressed in various human tissues - thymus and testis appear to express the highest levels.

Localisation

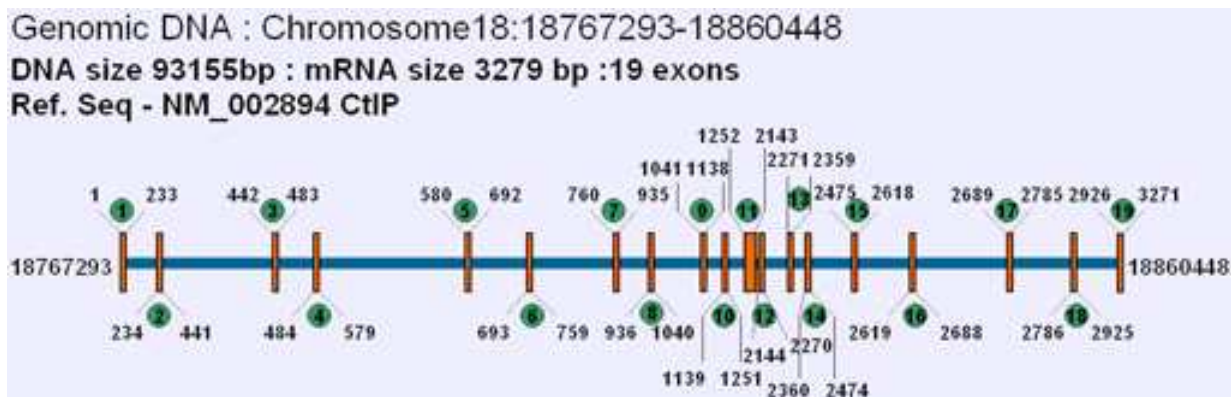
Predominantly localized in the nucleus; contains 4 potential nuclear localization signals and two leucine zipper motifs, a Rb binding domain, a CtBP binding motif, a coiled-coil domain, two CXXC motifs similar to the Zn-hook motif of Rad50.

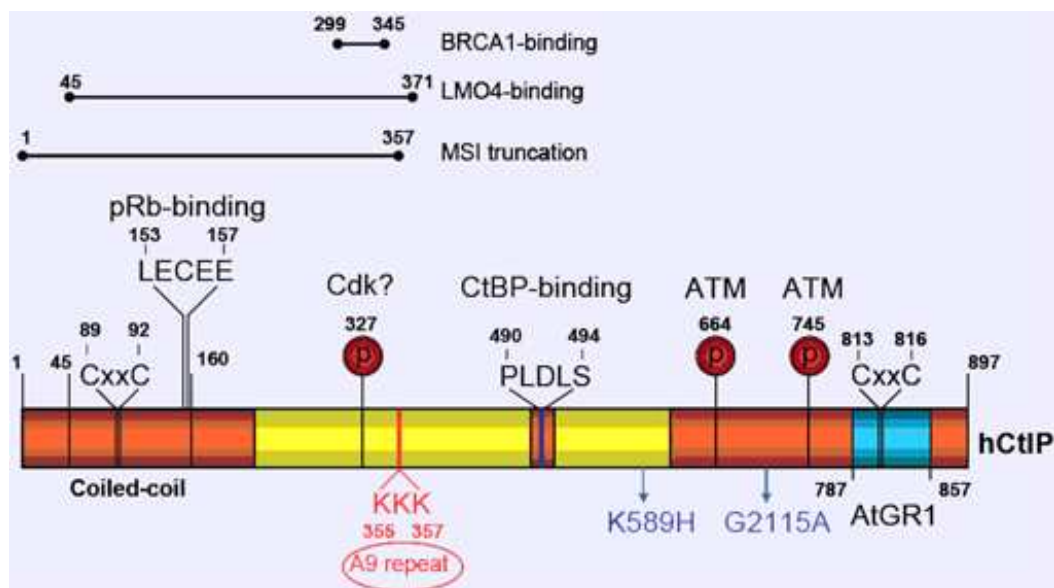
Function

Potential modulator of BRCA1 in transcriptional regulation, DNA repair and cell cycle checkpoint control.

Family: ezrin/radixin/myosin family.

Category: regulatory, transcription factor, antioncogene.





Domain structure of hCtIP. All known CtIP proteins contain a highly conserved CtBP-binding motif, two CXXC motifs and a phosphorylation site that corresponds to Ser327 in hCtIP. The Rb-binding motif is conserved only in mammalian CtIP. The N-terminal and C-terminal regions of all the CtIP homologs show high degrees of conservation. The ATM target site that corresponds to Ser664 is not conserved in CtIP of certain species (e.g., mouse and chicken). The A9 repeat, a tumor-specific nucleotide polymorphism (G2115A) and a nucleotide polymorphism (G1766A) resulting in an amino acid substitution (K589H) observed in tumor and normal cells are indicated. The region between amino acid positions 45 to 160 is a coiled-coil. A C-terminal region conserved between CtIPs and the plant (*Arabidopsis thaliana*) gamma response 1 (AtGR1) protein is also indicated (light blue).

Interaction: binds to Rb, CtBP, BRCA1, LMO4, SIAH1, Ikaros, MRE11 complex.

Homology

Homolog to *C.elegans* r05d3.4, fission yeast Ctp1. CtIP is conserved among vertebrates. A C-terminal domain of CtIP is homologous to plant gamma response 1 (AtGR1) protein of *Arabidopsis thaliana*.

Variant: CtIP splice variant (Genebank Accession # NP_976037) with 867 a.a. is identical to CtIP except the C-terminal region (a.a. 786-867).

Mutations

Germinal

Knockout mice experiment has shown that inactivation of both CtIP alleles resulted in early embryonic lethality at stage E4. However the heterozygous CtIP^{+/-} mice were viable with reduced life span due to development of multiple tumors.

Somatic

A number of human tumor cell lines derived from various tissues did not detect any homozygous deletion within the CtIP gene. However, some missense and silent mutations have been reported.

Implicated in

Tumors

Disease

Recent studies with mutant mice have raised the possibility that CtIP might be a tumor suppressor gene.

Inactivation of both CtIP alleles results in early embryonic lethality at stage E4. However, the heterozygous CtIP^{+/-} mice are viable, but the life span is reduced compared to CtIP^{+/+} animals due to the development of multiple tumors. Among the types of tumors observed in CtIP^{+/-} animals, B and T cell lymphomas (B-NHL and T-NHL) are most prevalent. Enhanced lymphoid specificity of tumorigenesis might reflect the fact that these tissues are active sites of DNA repair and CtIP insufficiency might contribute to lymphoma development due to potential defects in DNA repair.

Oncogenesis

Since CtIP seems to be very important for the activities of tumor suppressors such as BRCA1, pRb family and Ikaros family, CtIP may be a tumor suppressor protein.

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