

Gene Section

Mini Review

CKS1B (CDC28 protein kinase regulatory subunit 1B)

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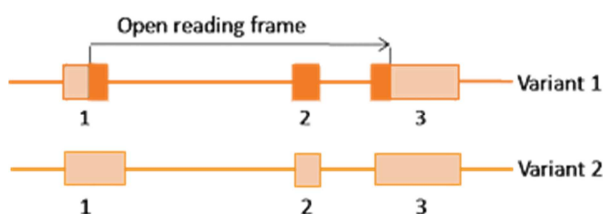
Identity

Other names: CKS-1; CKS1; PNAS-143; PNAS-16; PNAS-18; cks1

HGNC (Hugo): CKS1B

Location: 1q21.3

DNA/RNA



Genomic organization of the CKS1B gene.

Description

Three exons, spans approximately 4.61 kb of genomic DNA in the centromere-to-telomere orientation. The translation initiation codon ATG is located in exon 1, and the stop codon in exon 3.

Transcription

mRNA of approximately 1.8 kb. There are two transcript variants for CKS1B gene. The variant 2 uses a different splice site at the 3' end of the first exon compared to variant 1. There is no evidence that variant 2 encodes a protein.

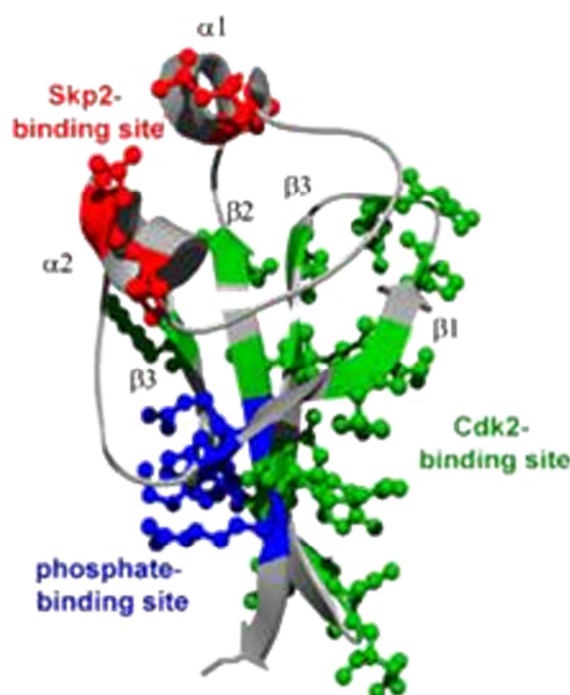
Pseudogene

4 processed, non-expressed, pseudogenes in human genome.

Protein

Description

The open reading frame encodes a 79 amino acid protein, with an estimated molecular weight of approximately 9660 Da.



The side chains of residues of CKS1b in the binding sites for Cdk2, Skp2 and phosphorylated substrate are shown, with residues in the Cdk2-binding site in green, in the phosphate-binding site in blue, and the Skp2-binding site in red. (The structure figure modified from the origin paper: Markus A. Seeliger et al, Role of Conformational Heterogeneity in Domain Swapping and Adapter Function of the Cks Proteins. J. Biol. Chem., Vol. 280, Issue 34, 30448-30459, August 26, 2005).

Expression

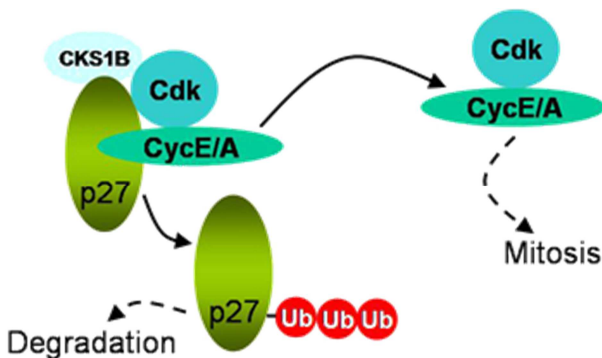
Basical level expression in all mammalian cell and aberrant expression in cancer cell.

Localisation

Cytoplasm and nucleus.

Function

CKS1B protein binds to the catalytic subunit of the cyclin dependent kinases and is essential for their biological function of cell cycle control.



Schematic of the regulation of cell cycle by the CKS1B. CKS1B associates with the p27kip1-Cdk/cyclin complex, induces the formation of the p27kip1-SCF ubiquitin ligase complex, triggers degradation of p27kip1, and signals cells to undergo the G1/S transition by releasing and activating the Cdk/cyclin A/E complexes. CycE/A, cyclin E or Cyclin A; Ub, ubiquitin.

Homology

The CKS1B proteins are evolutionary conserved. Mammalian cells express two well-conserved members, like the human CKS1B and CKS2 proteins. The CKSB1B protein is highly conserved across species.

Implicated in

Cancer

Note

The expression of CKS1B is elevated in multiple cancer, including breast cancer, lymphoma, myeloma, colon cancer, prostate cancer, lung cancer, renal carcinoma, oesophageal squamous cell carcinoma, salivary cancer, serous ovarian cancer, bladder cancer, urothelial carcinoma et al.

Prognosis

Overexpression of CKS1B is associated with poor prognosis in multiple cancer, including myeloma, breast cancer, lymphoma, renal carcinoma, ovarian cancer et al.

Oncogenesis

Amplification and overexpression of CKS1B were strongly associated with lymph node metastasis and poor prognosis in breast, salivary cancer and oesophageal squamous cell carcinoma. Generally, CKS1B is an essential factor in facilitating Skp2-dependent degradation of p27. In breast cancer cell,

overexpression of CKS1B may inhibit the apoptosis through the MEK-Erk pathway. All of these suggest that CKS1B alterations may have a significant biological role in the tumorigenesis in different tissue and the novel therapeutic strategy for cancer through inhibiting the CKS1B activity. Therefore, disruption of Skp2-CKS1B assembly or down-regulation of CKS1B expression may be used for cancer therapy.

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