Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Review

UBE2C (ubiquitin-conjugating enzyme E2C)

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Published in Atlas Database: June 2008

Online updated version : http://AtlasGeneticsOncology.org/Genes/UBE2CID44079ch20q13.html
DOI: 10.4267/2042/44473

Identity

Other names: UBCH10; UBE2C-PEN; UbcH10; dJ447F3.2; LOC11065

HGNC (Hugo): UBE2C

Location: 20q13.12

Local order: CENTROMERE---WFDC3-DNTTIP1-UBE2C-TNNC2-SNX21-ACOT8---TELOMERE.

Note: UbcH10 catalyzes the covalent attachment of ubiquitin to target proteins. It is required for the destruction of mitotic cyclins.

DNA/RNA

Description

UBE2C is located on chromosome 20, at 20q13.12 according to Entrez Gene. In AceView, it covers 4.40 kb, from 43874623 to 43879017 on the direct strand.

Transcription

There are 6 representative transcripts annotated in RefSeq database, but, according to AceView, Homo sapiens cDNA sequences in GenBank support at least 13 spliced variants. Isoform 1, the longest isoform, is composed of 6 coding exons of varying lengths, separated by introns: NM_007019.2 (mRNA-ubiquitin-conjugating enzyme E2C): mRNA product length: 823.

Protein

Description

The UbcH10 gene encodes a member of the E2 ubiquitin-conjugating enzyme family that is involved in the ubiquitin dependent proteolysis. In this pathway, ubiquitin-activating enzyme (E1), ubiquitin-conjugating enzyme (E2), together with ubiquitin ligase (E3), catalyze the covalent attachment of ubiquitin to target proteins, targeting them for degradation mediated by the 26S proteasome.

The full-length UbcH10 contains 179 residues for a 19.6 kDa weight. It belongs to the class III Ubc proteins that are characterized by an NH2-terminal extension followed by the "core" Ubc fold.

Like all E2 enzymes, UbcH10 contains an active site cysteine residue (position 114) that is crucial for the formation of the ubiquitin-thiolester. Alteration of this residue C(114)S strongly inhibits ubiquitination of cyclin A and Cyclin B confering a dominant-negative phenotype.

Levels of UbcH10 are modulated by autoubiquitination. This process is dependent on a motif, the "destruction box" [Arg-X-X-Leu-X-X-(Leu/Ile)-X-Asp] recognized by the mitotic-specific ubiquitination machinery.

A study suggests that a destruction box is present in the UbcH10 sequence and includes residues 129-132 (Arg-Thr-Ile-Leu). Interestingly an SNP is reported for the residue 129 (refSNP ID: rs7352110, alleles A/G, Arg>Gly).

Accession	Cluster Name	Members	Organisms	Length	Identity
UniRef90_O00762	Ubiquitin-conjugating enzyme E2 C	O00762	Homo sapiens (Human)	179	90%
		Q5TZN3	Pan troglodytes (Chimpanzee)		
		Q9BQP1	Canis familiaris (Dog)		
		UPI0000E256D5	Monodelphis domestica (Short-tailed gray opossum)		
		UPI0000E	Bos taurus (Bovine)		
		UPI00005EAD60	Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey)		
		Q32PA5	Mus musculus (Mouse)		
		Q4R9D1	Rattus norvegicus (Rat)		
		Q9D1C1	Macaca mulatta (Rhesus macaque)		

This would be important since any change in the putative destruction box could stabilize UbcH10 against destruction.

Expression

UbcH10 mRNA and protein are expressed at low levels in most adult normal tissues. In contrast, UbcH10 mRNA and protein are highly expressed in tumor tissues. Moreover, UbcH10 protein levels fluctuate during the cell cycle being abundant during M and early G1 phases, but decreasing in late G1, S and G2 phases.

Localisation

Nucleoplasm. Cytosol.

Function

UbcH10 is crucial for cell cycle progression during the G2/M phase, since its function is required for the destruction of mitotic cyclins and other mitosis-related substrates. UbcH10 interacts with the multiprotein complex APC (anaphase-promoting complex), which has E3 ubiquitin ligase activity, and targets for destruction substrates from the preceding mitosis (cyclin A, cyclin B, securin, geminin). Once these target proteins have been degraded, UbcH10 adds ubiquitins to itself, triggering its own destruction. As a result, the absence of UbcH10 allows the accumulation of cyclin A, which in turn contributes to the APC inactivation, providing a molecular switch that allows cells to proceed from cell division to a new round of DNA duplication. Hence, the function of UbcH10 is strictly linked to the progression of cell cycle through the M phase and the coupling of mitosis to S-phase entry via autonomous regulation of the anaphase-promoting complex.

Implicated in

Human cancers

Note

Several studies suggest a possible use of UbcH10 investigation (together with other molecular markers) in early detection of cancer. Other studies suggest that inhibition of UbcH10 could have a therapeutic potential in cancer treatment.

Disease

UbcH10 overexpression was reported in a number of human cancer cell lines and primary tumors and expression data strongly support an association between high UbcH10 expression and a poor tumor differentiation. Expression studies have also shown a correlation between UbcH10 overexpression and the proliferation status since there is a good association with the proliferation marker Ki-67/MIB1. It was found overexpressed in lung carcinoma (squamous and adenocarcinoma, poorly versus well differentiated), bladder carcinoma (grade 3 versus grade 2), prostate carcinoma (metastatic versus primary), gastric adenocarcinoma cervical, esophageal adenocarcinoma (adenocarcinoma versus Barrett's metaplasia), breast cancer (grade 3 versus grade 1, malignant versus benign neoplastic lesions), brain (astrocytomas versus low-grade tumors or normal controls), medulloblastoma, ovarian carcinoma (grade 3 versus grade 1 and 2), thyroid carcinoma (poorly versus well differentiated), adrenocortical gland, Wilms tumor (relapsed versus relapse-free) hepatocellular carcinoma (correlation with higher frequencies of invasion to capsular formation, invasion to portal vein and tumor de-differentiation). Several expression analysis and functional studies have also shown that UbcH10 resulted up-regulated in experimental model of carcinogenesis, that its overexpression leads to the acquisition of a malignant phenotype and that its knockdown successfully resulted in growth arrest.

Prognosis

It was seen that UbcH10 overexpression is a negative predictor of clinical outcome in patients affected by ovarian and hepatocellular carcinoma. Therefore, UbcH10 has been suggested as a helpful prognostic indicator for ovarian and hepatocellular carcinoma patients.

Oncogenesis

20q13.1 chromosomal region is frequently associated with genomic amplification in different malignant neoplasias and amplification of UbcH10 locus has been reported in the case of gastroesophageal carcinomas, colorectal carcinomas with liver metastases, cervical cancers, ovarian carcinomas, gliomas and culture cell lines obtained from anaplastic thyroid carcinomas.

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This article should be referenced as such:

Pallate P, Berlingieri MT, Fusco A. UBE2C (ubiquitin-conjugating enzyme E2C). Atlas Genet Cytogenet Oncol Haematol. 2009; 13(5):367-370.