

Gene Section

Mini Review

CDKN1B (cyclin-dependent kinase inhibitor 1 B)

Chrystèle Bilhou-Nabera

Laboratoire d'Hématologie, Hôpital du Haut-Lévêque, CHU de Bordeaux, Ave de Magellan, 33 604 Pessac, France

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Identity

Other names: KIP1; P27KIP1

Location: 12p13

Local order: centromere - CDKN1B - ETV6 - PRB - KCNA5 - CACNL1A1 - telomere.



CDKN1B (12p3) - Courtesy Mariano Rocchi.

DNA/RNA

Description

Coding region from two exons.

Transcription

2.5 Kb mRNA; CDKN1B gene regulation by extracellular antiproliferative signals occurs at a post-transcriptional level.

Protein

Description

198 amino-acids; 22 kDa; homology to WAF1, limited to a 60 amino acid segment in the N-term half of the protein (residues 28-88); putative bipartite nuclear localization signal near the C-term (153-169); C-term extension of 23 amino acids that contains a consensus Cdc2 phosphorylation site.

Expression

Expressed in all tissues tested; high levels in skeletal muscle, low levels in liver and kidney.

Localisation

Nuclear.

Function

- CDKN1B is a negative regulator implicated in G1 arrest mediated by TGF β , cell-cell contact, agents that elevate cyclic AMP and rapamycin; CDKN1B binds to and acts as a stoichiometric inhibitor of G1-cyclin-cyclin dependent kinase complexes (cyclin E-Cdk2, cyclin A-Cdk2, cyclin D-Cdk4 (restriction point)), controlling G1 to S phase transition or exit from the cell cycle; CDKN1B coordinates the varied inputs from the extracellular environment; post-translational ubiquitin-mediated proteasomal proteolysis represents the major regulatory influence of CDKN1B protein level.

- in CDKN1B knockout mouse, CDKN1B defect causes multi-organ hyperplasia with features of gigantism, abnormalities of thymus, retina, pituitary, adrenal glands and gonadal organs (ovulatory defect and female sterility).

Homology

Cip1/WAF1.

Implicated in

Haematological malignancies

Note: hemizygous interstitial deletion is found in 10% of cytogenetically normal ANLL; monoallelic deletion found in 5% ANLL cases, but not described in ALL; no case so far of CDKN1B mutations in leukemia samples.

Primary breast cancers

Prognosis

A low nuclear expression of CDKN1B protein is a significant predictor of poor disease-free survival; in contrary, high level of CDKN1B protein expression combined with low level expression of its target (cyclin E-Cdk2) correlates with about 90% 10-yr overall survival in the lymph node-negative subgroup.

Primary colorectal carcinomas

Prognosis

CDKN1B is an independent prognostic marker: low levels are significantly correlated with a poor prognosis.

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