Atlas of Genetics and Cytogenetics
in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

CDKN1A (cyclin-dependent kinase inhibitor 1A)

Delphine Javelaud, Françoise Besançon

Institut Curie, Pavillon Pasteur, Unité INSERM 365, 26 rue d'Ulm, 75231 Paris cedex 05, France (DJ, FB)

Published in Atlas Database: April 2001

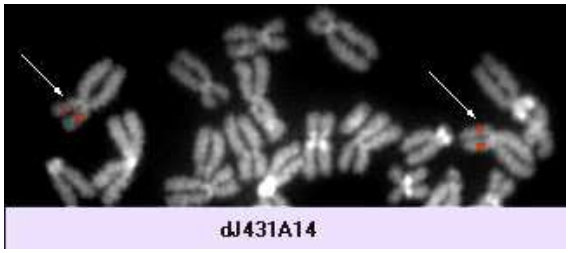
Online updated version: http://AtlasGeneticsOncology.org/Genes/CDKN1AID139.html
DOI: 10.4267/2042/37747

Identity

Other names: p21; WAF1 (Wild type p53 activated protein-1); CIP1 (CDK- interacting protein); SDI1 (Senescence cell- derived inhibitor-1); CAP20; MDA-6 (melanoma differentiation-asssociated protein-1)

HGNC (Hugo): CDKN1A

Location: 6p21.2



CDKN1A (6p21) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Description

3 exons (68, 450, 1600 pb ; the first exon is not translated).

Transcription

2,1 kb mRNA, expression regulated at both transcriptional and post-transcriptional levels.

Protein

Description

164 amino acids, 18 kDa. Contains interacting domains with several proteins (see Figure) and a nuclear localization signal.

Expression

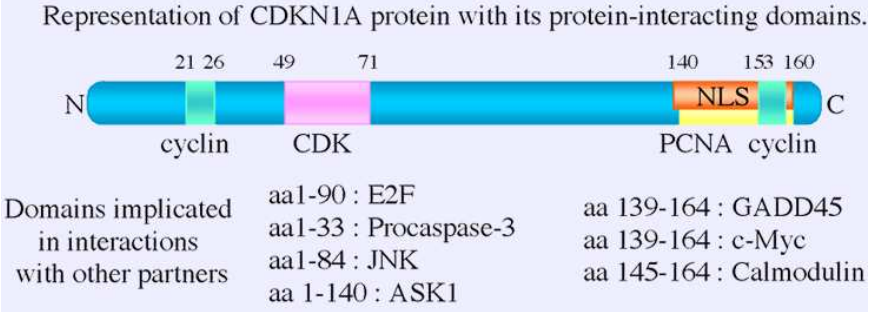
In all adult human tissues. CDKN1A expression in the developing mouse embryo is correlated with cell-cycle arrest that precedes terminal differentiation in a variety of tissues.

Localisation

Nuclear and cytoplasmic.
Located predominantly in the nucleus.
Relocalization to the cytoplasm during the differentiation of immature monocytes.

Function

Can interact with cytoplasmic proteins (pro-caspase-3, ASK-1, JNK, CaM, cyclinD-CDK4).



CDKN1A is implicated in regulation of cell growth and cell response to DNA damage. It inhibits cell cycle progression in G1 by binding to G1 cyclin-CDK complexes and to PCNA antigen and may also induce G2 arrest. In response to DNA damage p53 induces CDKN1A expression, which is responsible for the cell cycle arrest at the G1 checkpoint. CDKN1A plays also a role in the protection of cells against apoptosis and its expression is essential to maintain cell survival during differentiation of several cell lineages.

Homology

With p27kip1 and p57kip2 in the N- terminal.

Mutations

Somatic

Analysis of normal and tumor cells revealed two common variants in the CDKN1A gene which were not unique to tumors: a C to A substitution at codon 31 (Ser 31-to-Arg) which does not result in loss of activity and a C to T change in the 3' untranslated region of the CDKN1A gene, 20 bp following the stop codon. In prostate cancer, a single base insertion at codon 35, resulting in frameshift, protein troncation and impairement of activity, has been identified. A Phe to Leu change at codon 63, an Arg to Trp change at position 94 and an Asn to Ser change at position 50 were observed in a Burkitt's lymphoma, a human breast carcinoma and a malignant melanoma cell line, respectively.

References

Harper JW, Adami GR, Wei N, Keyomarsi K, Elledge SJ. The p21 Cdk-interacting protein Cip1 is a potent inhibitor of G1 cyclin-dependent kinases. Cell. 1993 Nov 19;75(4):805-16

Harper JW, Adami GR, Wei N, Keyomarsi K, Elledge SJ. The p21 Cdk-interacting protein Cip1 is a potent inhibitor of G1 cyclin-dependent kinases. Cell. 1993 Nov 19;75(4):805-16

Chedid M, Michieli P, Lengel C, Huppi K, Givol D. A single nucleotide substitution at codon 31 (Ser/Arg) defines a polymorphism in a highly conserved region of the p53-inducible gene WAF1/CIP1. Oncogene. 1994 Oct;9(10):3021-4

Mousses S, Ozçelik H, Lee PD, Malkin D, Bull SB, Andrulis IL. Two variants of the CIP1/WAF1 gene occur together and are associated with human cancer. Hum Mol Genet. 1995 Jun;4(6):1089-92

Parker SB, Eichele G, Zhang P, Rawls A, Sands AT, Bradley A, Olson EN, Harper JW, Elledge SJ. p53-independent expression of p21Cip1 in muscle and other terminally differentiating cells. Science. 1995 Feb 17;267(5200):1024-7

Gartel AL, Tyner AL. The growth-regulatory role of p21 (WAF1/CIP1). Prog Mol Subcell Biol. 1998;20:43-71

Asada M, Yamada T, Ichijo H, Delia D, Miyazono K, Fukumuro K, Mizutani S. Apoptosis inhibitory activity of cytoplasmic p21(Cip1/WAF1) in monocytic differentiation. EMBO J. 1999 Mar 1;18(5):1223-34

Gartel AL, Tyner AL. Transcriptional regulation of the p21((WAF1/CIP1)) gene. Exp Cell Res. 1999 Feb 1;246(2):280-9

Dotto GP. p21(WAF1/Cip1): more than a break to the cell cycle? Biochim Biophys Acta. 2000 Jul 31;1471(1):M43-56

This article should be referenced as such:

Javelaud D, Besançon F. CDKN1A (cyclin-dependent kinase inhibitor 1A). Atlas Genet Cytogenet Oncol Haematol. 2001; 5(3):170-171.