Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

RB1 (retinoblastoma)

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Published in Atlas Database: September 1999

Online updated version : http://AtlasGeneticsOncology.org/Genes/RB1ID90.html
DOI: 10.4267/2042/37533

Identity

Other names: human retinoblastoma suspectibility gene

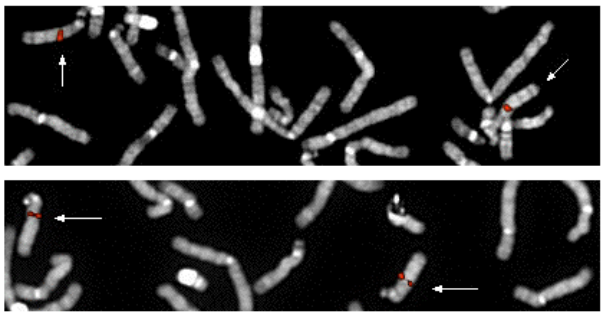
HGNC (Hugo) : RB1

Location : 13q14

DNA/RNA

Description

27 exons spanning 180 kb.



c-RB1 at 13q14 in normal cells: PAC 825K22 (top) and PAC 971H14 (bottom) - Courtesy Mariano Rocchi.

Transcription

4.7 kb mRNA, 2.7 kb open reading frame, 2 kb 3'-UTR.

Protein

Description

928 aa nuclear phosphoprotein; 110 kDa; pRB is phosphorylated by members of the cyclin-dependent kinase (cdk) system prior to the entry into S-phase; hypophosphorylated pRB binds to members of the E2F family of transcription factors; binding to E2F is mediated by by two domains within pRB (pocket domains).

Expression

Ubiquitous.

Localisation

Nucleus.

Function

Cell cycle regulation, differentiation.

Homology

pRB, p107, and p130 constitute a small family of nuclear proteins with significant sequence similarity in two discontinuous areas (pockets domains); conditional on the phosphorylation status, these pocket proteins can bind transforming proteins of DNA tumor viruses as well as nuclear proteins.

Mutations

Germinal

Germline mutations in the RB1 gene are causative for hereditary predisposition to retinoblastoma; the spectrum of predisposing mutations includes large deletions (about 20%), single base substitutions (about 50%) and small length mutations (about 30%); most mutations are associated with almost complete penetrance: some rare alleles show incomplete penetrace and reduced expressivity (low penetrance retinoblastoma).

Somatic

In retinoblastomas, both RB1 alleles are mutated; in addtion to the mutational spectrum of germinal mutations, retinoblastomas can show loss of heterozygosity and hypermethylation at the CpG-island associated with the 5Œ-end of the RB1 gene.

Implicated in

Retinoblastoma

Disease

Hereditary predisposition to retinoblastoma formation in carrieres of a germinal mutation. Somatic inactivation of both RB1 alleles can result in sporadic unilateral retinoblastoma.

Sarcomas

Disease

Carriers of a germinal RB1gene mutation are predisposed to soft tissue sarcomas and osteogenic sarcomas. Somatic inactivation of both RB1 alleles observed in some sarcomas

Various cancers

Disease

RB1 gene mutations have been observed in several tumor entities. In lung cancer there is a notable high frequency of RB1 gene mutations although no increased incidence of these tumors has been observed in carriers of a germinal RB1 gene mutation.

References

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This article should be referenced as such:

Lohmann DR. RB1 (retinoblastoma). Atlas Genet Cytogenet Oncol Haematol. 1999; 3(3):137-138.