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Gene Section
Mini Review

BLM (Bloom)

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Identity

HGNC (Hugo): BLM

Location: 15q26.1

DNA/RNA

Transcription

4.4kb mRNA.

Protein

Description

1417 amino acids; ATP binding in amino acid 689-696; DEAH box in 795-798; two putative nuclear localization signals in the C-term in 1334-1349.

Expression

Accumulates to high levels in S phase of the cell cycle, persists in G2/M and sharply declines in G1. Hyperphoshorylated in mitosis.

Localisation

Nuclear (PML nuclear bodies and nucleolus).

Function

3'-5'DNA helicase; probable role in DNA replication and double-strand break repair.
Preferred substrates: G-quadruplex DNA, D-loops structures and X-junctions.
Recombinant protein promotes ATP-dependent branch migration of Hollyday junctions, effects, with topoisomerase III?, the resolution of a recombination intermediate containing a double Holliday junction with no flanking sequence exchanges, and possess a strand pairing activity.
Recombinant BLM possesses a strand pairing activity.
Participates in a supercomplex of BRCA1 -associated proteins named BASC (BRCA1-Associated genome Surveillance Complex) containing ATM (defective in ataxia telangiectasia), NBS1 (defective in Nijmegen syndrome) and MRE11 (defective in ataxia-telangiectasia-like disorder), MLH1, MSH2 and MSH6, which are involved in human non-polyposis colorectal cancer, RAD50 and DNA replication factor C.
Participates in a complex named BRAFT (BLM, RPA, FA, Topoisomerase III) containing five of the Fanconia Anemia (FA) complementation group proteins (FANCA, FANCG, FANCC, FANCE and FANCF).
Interacts physically and/or functionally with p53, 53BP1, WRN, MLH1, RAD51, TRF2, ATR, the largest subunit of CAF-1, ligase IV, FEN1, Mus81, the monoubiquitinated FANCD2 isoform.
Is Associated with telomeres and ribosomal DNA repeats.
Is phosphorylated in mitotic cells through the cdc2 pathway, and in response to DNA damaging agents or stalled replication forks.

Homology

Homologous to RecQ helicases, a subfamily of DExH box-containing helicases; in particular, similarity with the four known human members in the RecQ subfamily, human RecQL, human Wrn, the product of the Werner syndrome gene, and the human RecQL4, involved in the Rothmund-Thomson syndrome, and RecQL5 proteins.

Mutations

Germinal

Five BLM mutations introducing amino acid substitutions and four BLM mutations introducing premature nonsense codons into the coding sequence have been described to date; one BLM mutation consisting in a 6 bp deletion accompanied by a 7 bp insertion at nucleic acid position 2281 is common in patients from Ashkenazi Jewish ancestry, leading to a truncated protein of 739 amino acids in length; two BLM mutations, 631delCAA and 1610insA were detected in japanese patients.

Implicated in

Bloom syndrome

Disease

Bloom syndrome is a chromosome instability syndrome/cancer prone disease (at risk of numerous, early occurring cancers of various types).

Prognosis

1/3 of patients are dead at mean age 24 yrs, and the mean age of the 2/3 remaining alive patients is 22 yrs.

Cytogenetics

Chromatid/chromosome breaks; triradial and quadriradial figures, highly elevated spontaneous sister chromatid exchange rate.

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