

Gene Section

Mini Review

BARD1 (BRCA1 associated RING domain 1)

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Identity

Hugo: BARD1

Other names: BRCA1-associated RING domain protein 1

Location: 2q35

Local order: Antiparallel.

DNA/RNA

Description

The gene spans 81 kb, composed of 11 exons. Alternatively spliced isoforms are identified.

Insert known isoforms:

BARD1beta (rat testis);

BARD1delta (rat ovarian cancer cells);

BARD1delta (HeLa);

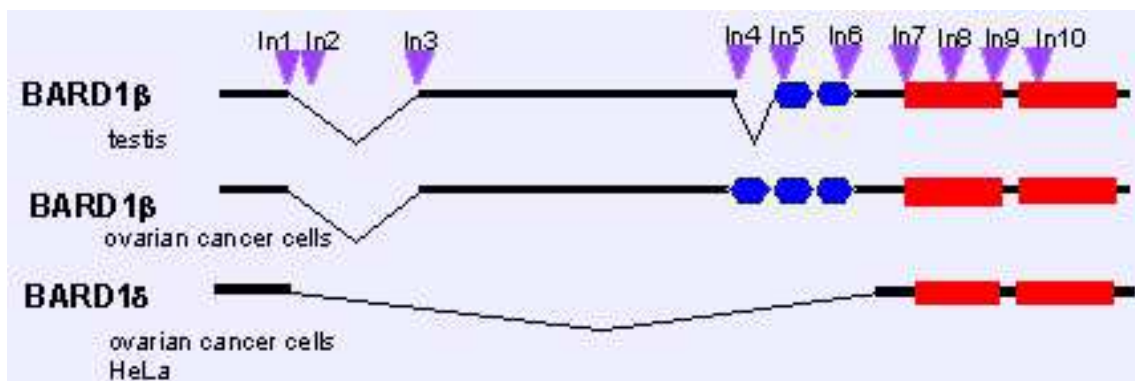
BARD1delta (rat ovarian cancer cells).

Transcription

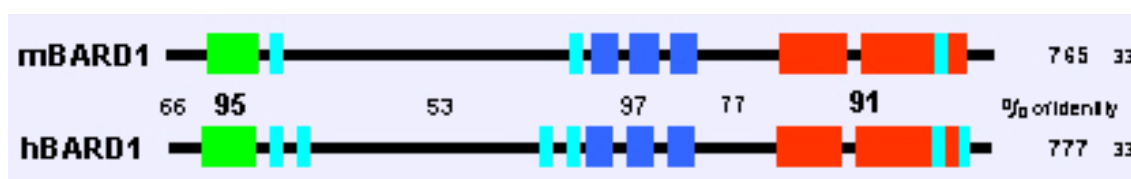
Transcription start is 100 bp upstream of first ATG of the BARD1 ORF. There are two 3' ends reported and possibly two alternative polyadenylation sites. BARD1 is expressed in most proliferative tissues. Highest expression in testis and spleen. No expression in the central nervous system.

Pseudogene

No pseudogenes reported.



BARD1 structure is presented with RING finger (green) ankyrin repeats (ANK, blue) and BRCT domains (red). Positions of introns (in) are indicated. Structures of splice variants are shown for BARD1beta from the rat (Feki et al., 2004), BARD1delta (Feki et al., 2005; Tsuzuki et al., 2006).



Mouse and human BARD1 protein sequences are shown schematically. RING finger domains (green), Ankyrin repeats (ANK, blue), BRCT domains (red), nuclear localization signals (light blue). Homology between human and mouse BARD1 is indicated in percentage of identical amino acids for structural regions.

Protein

Description

Human BARD1 777 amino acids; Structural motifs: RING, 5 Ankyrin repeats, 2 BRCT domains.

Expression

In the mouse BARD1 is expressed in most proliferative tissues. Highest expression in testis and spleen, no expression in nervous system.

During mouse development BARD1 is expressed in early embryogenesis and declines after day 9.

Localisation

During S-phase BARD1 localizes to nuclear dots. Partially, BARD1 is also localized to the cytoplasm in response to stress.

Function

BARD1 functions as heterodimer with BRCA1 as ubiquitin ligase. Several targets of the BARD1-BRCA1 ubiquitin ligase have been identified and suggest its implication in DNA repair, polyadenylation, cell cycle control, and mitosis.

BARD1 acts as inducer of apoptosis, independently of BRCA1, by binding to p53, and by binding to the stress

response kinase DNA-PK, facilitating p53 phosphorylation and stabilization. Thus BARD1 acts as signaling molecule from genotoxic stress towards p53-dependent apoptosis.

Homology

BARD1 is homologous to BRCA1, regarding the N-terminal RING finger and the C-terminal BRCT domains. Weak homology between BARD1 and BRCA1 can be found throughout exon 1 to exon 4, and from exon 7 through exon 11, with conserved intron-exon junctions.

Mutations

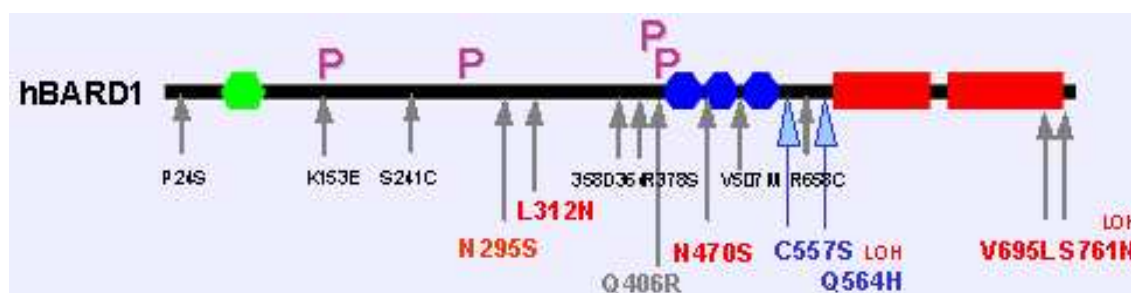
Note: Several mutations of BARD1 have been identified in breast and ovarian cancers. Three mutations have been reported associated with inherited predisposition to breast and ovarian cancer.

Germinal

Germline mutations were reported for C557S and Q564H.

Somatic

Several somatic mutation were reported in addition to C557S and Q564H.



BARD1 mutations associated with cancer. Small mutations are not unambiguously identified as cancer causing mutations, long arrows red labeled mutations are accepted as cancer associated. Blue indication maps germ line mutations. Q406R, might be cancer associated.

Implicated in

Breast and/or ovarian cancer

Note: Upregulated expression of truncated BARD1 in epithelial cancers.

Prognosis

Upregulated BARD1 is correlated with poor prognosis in breast and ovarian cancer.

Cytogenetics

No determined.

Hybrid/Mutated Gene

Not determined.

Abnormal Protein

No fusion proteins reported.

Ovarian cancer

Prognosis

Upregulated BARD1 is correlated with poor prognosis in breast and ovarian cancer.

Hybrid/Mutated Gene

No.

Abnormal Protein

No fusion proteins reported.

Lung cancer

Prognosis

Upregulated BARD1 is correlated with poor prognosis in breast and ovarian cancer.

Hybrid/Mutated Gene

No.

Abnormal Protein

No fusion proteins reported.

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