Some pathogenic BRCA1 mutants do not bind BARD1

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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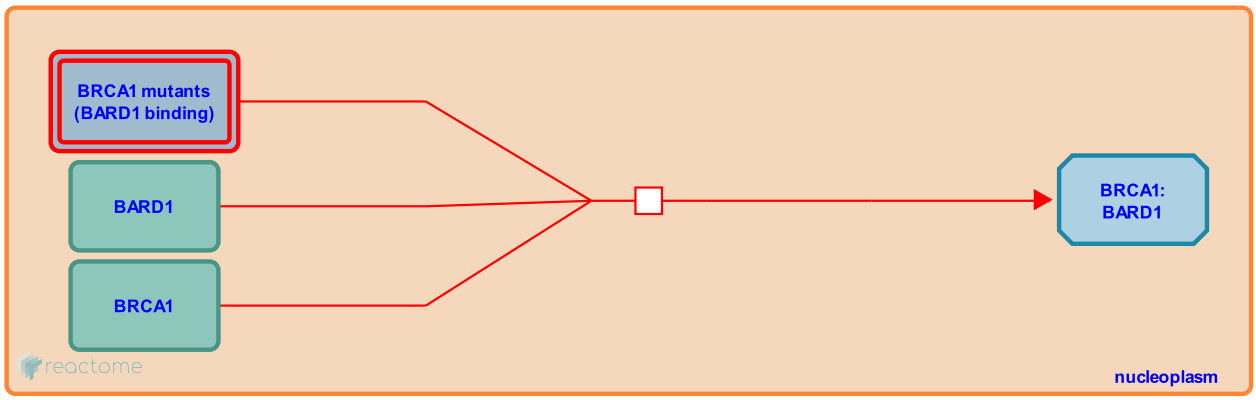
Stable identifier: R-HSA-9663194

Type: transition

Compartments: nucleoplasm

Diseases: cancer



The heterodimerization of BRCA1 and BARD1 is mediated by sequences encompassing the N-terminal RING domains of both proteins (Wu et al. 1996, Brzovic, Rajagopal et al. 2001, Brzovic, Meza et al. 2001, Morris et al. 2002). Cancer-predisposing mutations in the RING domain of BRCA1 frequently disrupt the formation of the BRCA1:BARD1 complex.

The following BRCA1 mutants identified in cancer patients or in families with the hereditary breast and ovarian cancer syndrome were functionally tested and shown to be unable to bind to BARD1:
BRCA1 M18T (Ransburgh et al. 2010)
BRCA1 C24R (Ransburgh et al. 2010)
BRCA1 C27A (Ransburgh et al. 2010)
BRCA1 T37R (Ransburgh et al. 2010)
BRCA1 C39Y (Ransburgh et al. 2010)
BRCA1 H41A (Ransburgh et al. 2010)
BRCA1 H41R (Ransburgh et al. 2010)
BRCA1 C44F (Ransburgh et al. 2010)
BRCA1 C47G (Ransburgh et al. 2010)
BRCA1 C61G (Wu et al. 1996, Ransburgh et al. 2010)
BRCA1 C64G (Wu et al. 1996, Ransburgh et al. 2010)
BRCA1 C64R (Caleca et al. 2014).

The following BRCA1 mutants were identified in cancer and predicted to be pathogenic. They are annotated as candidate mutants for BARD1 binding deficiency based on sequence similarity with the functionally characterized missense mutants (the same amino acid residue affected by a missense mutation as in a missense mutant shown to be unable to bind to BARD1) or based on the truncation of the RING domain due to frameshift mutations:
BRCA1 C24F
BRCA1 H41Q
BRCA1 C61Y
BRCA1 Q12Tfs*5
BRCA1 E23Afs*18
BRCA1 E23Rfs*18
BRCA1 E23Vfs*17

Literature references

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Editions

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