Structural insights into perturbations in the interactions between the BRCA1-BRCT domains and BACH1 in breast cancer

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INTRODUCTION

Breast cancer is a type of c. in which cells in breast tissue change and divide,cancer begin in the lobules (milk glands) or in the ducts that connect the lobules to the nipple.Breast cancer is on the rise, both in rural and urban India. A 2018 report of Breast Cancer statistics recorded 1,62,468 new registered cases and 87,090 reported deaths. Cancer survival becomes more difficult in higher stages of its growth, and more than 50% of Indian women suffer from stage 3 and 4 of breast cancer.Metastatic breast cancer is one of the most devastating cancers that have no cure. Many therapeutic and diagnostic strategies have been extensively studied in the past decade. Among these strategies, cancer nanotechnology has emerged as a promising strategy in preclinical studies by enabling early identification of primary tumors and metastases, and by effective killing of cancer cells by Qingxin Mu et al.The major unresolved problems with metastatic breast cancer is recurrence after receiving objective response to chemotherapy, drug-induced side effects of first line chemotherapy and delayed response to second line of treatment. Unfortunately, very few options are available as third line treatment.by Dona sinha et al

BRCA1 (Breast-Cancer susceptibility gene 1) and BRCA2 are tumor suppressor genes, the mutant phenotypes of which predispose to breast and ovarian cancers. Intensive research has shown that BRCA proteins are involved in a multitude of pivotal cellular processes. In particular, both genes contribute to DNA repair and transcriptional regulation in response to DNA damage by Yoshida K et al.2004.Germline mutations in the *BRCA1* tumor suppressor gene often result in a significant increase in susceptibility to breast and ovarian cancers. Mutations are known to target the highly conserved C-terminal BRCT repeats that function as a phosphoserine/phosphothreonine-binding module.

EXPERIMENTALS

To understand in detail about breast cancer using computational tools a BRCA1 structure was downloaded from protein data bank(PDB ID:1T15.Initial structures appeared in PDB are 9574.Homo sapiens 6938 structures.Experiment method structures appeared are, X-ray diffraction-6461,Electron microscopy 241,Solution NMR 234 structures.After checking on refinement solution (1.5-2.0) 2171 structure appeared.Finally after checking for Latest updates 209 structures appeared.Expression system used E.coli,Method performed X-Ray Diffraction.Resolution is 1.85,R-Valuefree is 0.222,R-Valuework is.0.206.In order to determine the quality of structure two tests are performed,checking one tenth of resolution and difference between R-work and R-free.Analysis of macro and micro molecule(ID:SEP),secondary structures are performed which is followed by analysis of number of polar contacts and their bond length using PyMOL.

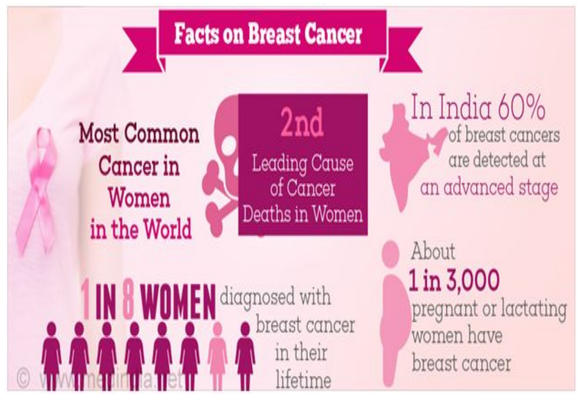

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Figure 1 Present ceneriao of present in india as of October 8 2020

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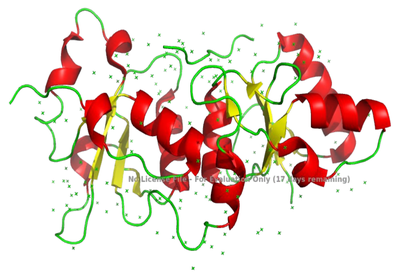

Figure 2 The three dimensional of BRCA1-BRCT showing alpha-hestructure lices and beta-strands

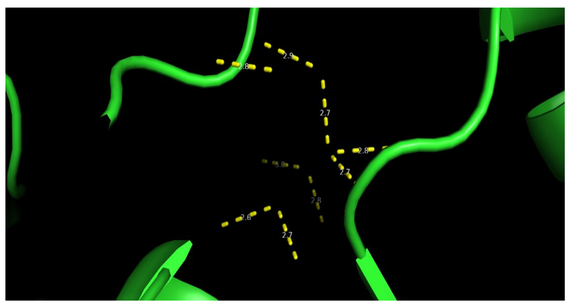

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figure 3 The three dimensional structure showing polar contacts and their bond lengths

RESULTS & DISCUSSION

After performing the quality tests one tenth of resolution is lesser than R-work and the difference between R-work and R-free is lesser than 0.05, therefore the structure is good quality .Then analysis of structure (PDB ID 1T15) in PyMOL showed 11 alpha-helices and 10 beta-strands. The structure showed 9 polar contacts,with an average bond length of 2.7.After changing the colour of chains by secondary structure by helix sheet it showed Green coloured structure and a Cyan coloured structure in PYMOL.The report of X-ray crystal structure at a resolution of 1.85 Å of the BRCA1 tandem BRCT domains in complex with a phosphorylated peptide representing the minimal interacting region of the DEAH-box helicase BACH1. The structure reveals the determinants of this novel class of BRCA1 binding events.It is showed that a subset of disease-linked mutations act through specific disruption of phospho-dependent BRCA1 interactions rather than through gross structural perturbation of the tandem BRCT domains provided by Clapperton et al

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