ABSTRACT

BRCA1 is a tumor suppressor gene that encodes 1863 amino acid protein having important role in genome stability by DNA repair mechanism. BRCT domain is located at the C terminal of BRCA1 and is critical for the interactions between BRCA1 and its binding partners. Mutations in BRCT domain of BRCA1 are reported in several types of cancers. In this study we attempted to find out functional consequences of 4 selected mutations in BRCT domain by bioinformatics analysis and cloned BRCT and full length *BRCA1* gene for the evaluation of BRCA1 functions. R1699Q, A1708V, T1837R and T1837C mutations were selected from the literature and analyzed by Polyphen-2, ConSurf, MutPred and SWISS Model. For cloning *BRCA1* and BRCT domain were PCR amplified from human cDNA, cloned in CMV-eGFP vector and sequenced. Bioinformatics analysis showed that all four mutations have highly damaging potential and can alter the normal role of BRCA1 in the cell. Homology based 3D models of BRCT domain indicated the location of each variant while it was also found that all four residues are highly conserved. It was concluded that these mutations can be highly deleterious and can lead to disturb the genome stability in the cell however; functional assays are needed to confirm these predictions.