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Structural effect of P278A mutation conferring breast cancer susceptibility in the p53 DNA-binding core domain

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One of the common malignancies faced by women around the world is breast cancer. Risk factors for breast cancer include both genetic and non-genetic. Variants in some of the candidate genes are a common risk factor in breast cancer. These genetic variants associated with breast cancer can be classified as high, moderate or low based on relative risk [1]. Among them, genes that predispose to high risk for breast cancer include *TP53*, *BRCA1*, *BRCA2*, *PTEN*, *STK11* and *CDH1*. A large number of studies have assessed the prognostic and predictive role of TP53 alterations in breast cancer. It is well known that *TP53* is mutated in about 30% of breast cancers [2]. We have analyzed the genetic variation that may alter the expression and function of the *TP53* gene using the sequence-homology-based SIFT tool [3] and a structure-based approach using the PolyPhen-2 server [4]. These two computational approaches showed that rs17849781 (P278A) has a deleterious phenotypic effect conferring to breast cancer. Further, we have analyzed the structural effect of the P278A mutation in the p53 DNA-binding core domain by employing different computational methods.

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