

# **Assessing the Added Value of Breast Tumor Markers in Breast Cancer Genetic Risk Prediction Model BRCAPRO**

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## **Abstract**

BRCAPRO is a widely used genetic risk prediction model for estimating the carrier probabilities of mutations in BRCA1 and BRCA2 genes. BRCAPRO has been enhanced to utilize information on molecular markers ER, PR, CK5/6, and CK14. However, no independent validation study on the utility of these markers in risk prediction exists to support using these enhanced features in actual clinical settings. Further, an important predictive and prognostic marker for breast cancer, Her-2/neu (Her2) is not utilized in BRCAPRO. To fill in these gaps, we carried out a study with the goals: (1) incorporate Her2 in BRCAPRO; (2) conduct a validation study of the markers. We used the data from the UT MD Anderson Cancer Center's breast clinic for this study. To avoid bias, separate sets of data were used for model building with Her2 (409 probands) and validation (796 families). We ran BRCAPRO on three settings: (1) no marker data used; (2) ER/PR used; and (3) ER/PR and Her2 used. Our results show that ER/PR substantially improves discrimination between BRCA1 and BRCA2 mutation carriers. Further inclusion of Her2 in the model helps discriminate between carriers and non-carriers of BRCA mutations.

**Keywords:** Breast cancer; BRCAPRO; BRCA1; BRCA2; Risk prediction; Tumor markers; Carrier probability.

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