Title. BRCA1 and BRCA2 Mutations in an Ethnically Diverse Cohort of High-Risk Women: A Comparison Between African-American and Caucasian Families

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Purpose. To determine the spectrum and frequency of BRCA1 and BRCA2 gene mutations among individuals from ethnically diverse high-risk families and characterize the differences and/or similarities between clinical predictors of mutations in African-American (AA) and Caucasian-American (CA) families with hereditary breast cancer.

Patients and Methods. Families were identified through probands who presented at hospital-based cancer risk clinics. DNA testing for BRCA1/2 was offered to families with at least two or more cases of breast and/or ovarian cancer among 1st- and 2nd-degree relatives. For each family, the individual with the highest probability of being a mutation carrier was selected for testing.

Results. One hundred fifty-five high-risk families were screened for BRCA1/2 mutations. Seventy-eight were CA; 43 were AA; 29 were Ashkenazi Jewish (AJ); 2 were Hispanic; and 2 were Asian. Genetic susceptibility to breast cancer could be explained by deleterious BRCA1 mutation, while 16.7% were found to have a deleterious BRCA2 mutation. The incidence of BRCA1 mutations among the AA families was roughly half that among CA families (16.3% vs 30.8%), and the incidence of BRCA2 mutations was also lower (11.6% vs 15.4%). As expected, AJ families had even higher rates of either mutation than CA families (41.4% for BRCA1 and 27.6% for BRCA2). For all families combined, the likelihood of having either mutation was strongly associated with the number of breast/ovarian cancer cases among 1st- and 2nd-degree relatives and early age of onset of breast cancer. BRCAPro performed as well in AAs as it did in families of other ethnic origins.

Conclusions. These results suggest that BRCA mutations occur in women of diverse ethnic backgrounds. When the entire coding regions of both BRCA1/2 genes are analyzed in carefully selected high-risk families, a high percentage of tests will be positive for deleterious mutations. BRCA1/2 mutation study should be an integral part of comprehensive cancer risk management, without regard to the ethnic origin of the proband. Although the BRCAPro computer model was developed principally for CA families, it is a useful tool in the AA population as well.