BRCA1 susceptibility markers and postmenopausal breast cancer: The Iowa Women's Health Study

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摘要

Abstract

Much research on early-onset breast cancer families has been performed and has shown that breast cancer in many of these families is linked to either BRCA1 or BRCA2. Fewer studies have examined the role of genetic predisposition in postmenopausal breast cancer. A nested case-control family study of breast cancer was conducted within the Iowa Women's Health Study, a population-based prospective study of 41,836 postmenopausal women. Probands were 251 incident cases diagnosed between 1988 and 1989. Three-generation pedigrees were developed through mailed questionnaires. From this collection of pedigrees, thirteen were identified for more detailed genetic analysis. Sibling-pair linkage analyses were performed using polymorphic markers in candidate regions in these 13 families with multiple cases of breast and other cancers. Four of the DNA markers are located on chromosome 17, and two of these (D17S579 and THRA1) flank the BRCA1 locus. Significant evidence for linkage to D17S579 was obtained in the total sample, in a model without inclusion of covariates or age at onset (P = 0.005), and in a model adjusted for five measured covariates and for variable age at onset (P = 0.008). Complete sequencing of the BRCA1 gene in these families, including all intron/exon boundaries, failed to reveal any mutations in 24 women with breast cancer from the 13 families. These data suggest that in some families identified by postmenopausal breast cancer cases, breast cancer risk may be mediated by a gene (or genes) in the BRCA1 region, but not BRCA1 itself.