The breast and ovarian cancer susceptibility gene BRCA1 contains an unusually high density (41.5%) of Alu elements. The homology between these repetitive Alu sequences can promote ectopic or homotypic homologous recombination. Ectopic homologous recombination, such as that reported in the BRCA1 gene, leads to large genomic rearrangements, which subsequently may cause disease phenotypes. In the BRCA1 gene, a number of different Alu mediated rearrangements, ranging from 510 bp to 23.8 kb, have been found to date. Two of them, a 510 bp deletion of exon 22 (IVS21-36del510) and a 3835 bp deletion of exon 13 (IVS12-1643del3835), are founder mutations in Dutch breast cancer patients and represent 36% of all BRCA1 mutations in this population. An additional recurrent founder mutation, a 6 kb duplication of exon 13 (ins6kbEx13), was detected mainly in English speaking countries.

We tested German families with a strong history of breast and ovarian cancer for mutations in the BRCA1 and BRCA2 genes by direct sequencing and DHPLC. In 270 investigated families, we detected 48 families in a study of the “German Consortium for Hereditary Breast and Ovarian Cancer” to establish a BRCA1/2 mutation profile and to determine family types with high frequencies of particular mutations. The included families are grouped into six categories depending on the family history. In fact, the families described here with a rearrangement in the BRCA1 gene are in the most severe categories with respect to their family history (B19, group A1 and B18, group B). Up to now the deletion IVS21-36del510 comprising exon 22 has exclusively been detected in Dutch breast cancer patients. The duplication ins6kbEx13 was mainly found in English speaking countries, except two reported cases from countries that have trading or other historical links with Britain, Belgium and Portugal. Consequently, family BN8 is the third family carrying the ins6kbEx13 duplication from a non-English speaking country. These newly described German cases support a recommendation to BRCA1/2 diagnostic laboratories to more generally implement tests for these specific rearrangements as well as other conceivable rearrangements within the BRCA1 gene.

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