Juan Dong
Dr. med.

Molekulare Analyse des BRCA1-Gens in 61 deutschen Familien mit Mamma- und Ovarialkarzinomen

Geboren am 2. 6.1960 in Harbin, China
Reifprüfung am Juli, 1978 in Harbin, China
Studiengang der Fachrichtung Medizin vom SS 1978 bis SS 1983
Staatsexamen am 25, Juli 1983

Promotionsfach: Humangenetik
Doktormutter: Frau Prof. Dr. Brigitte Royer-Pokora

Summary

61 German breast and/or ovarian cancer families were analyzed for mutations in the *BRCA1* gene. PCR-SSCP was used as a screening method and the SSCP variants were verified by sequencing. Allele specific oligonucleotide hybridization (ASO) was used to detect the 5382insC and restriction digestion of PCR product to detect the 5622 C>T mutation.

Mutations in the *BRCA1* gene were detected in 17 of 61 families (27.8%) in this study. The detection rate in different subgroups of the families was: 39% in families with breast and ovarian cancer, 18% in families with breast cancer only, 13% in families with 1-3 cases of breast/ovarian cancer, 42% in families with at least 4 cases of breast/ovarian cancer, 18% in families without bilateral breast cancer and 53% in families with bilateral breast cancer cases.

The characteristics of the mutations were: 16 truncation mutations (8 frameshift, 6 nonsense and 2 splice variants) and one missense mutation. The location of the mutation in the *BRCA1* gene was: 13 at the 3' third of the gene between the end of exon11 to exon 24 and 4 in the rest of the gene. Two mutations, the 5382insC and 5622C>T, occurred in two apparently unrelated families. The genotype of the 5382insC in both families is compatible with the rare haplotype shown to segregate with the 5382insC mutation in Canadian, American and British families.

No tendency for the mutations located at the 5' end in breast-ovarian cancer families was observed, but it was noticed that a higher ratio of ovarian cancer occurred in families with mutations at the 5' end of the gene. A risk associated with *BRCA1* mutations for other cancers cannot be determined in this study.

This study shows that *BRCA1* mutations can be found with a high probability in large German breast/ovarian cancer families with a relatively early onset of cancer. A slight trend towards a younger average age at diagnosis of breast cancer with successive generations in families with and without mutations was observed.