

Genetic testing for susceptibility to breast and ovarian cancer

Background:

Breast cancer is one of the most common malignancies in women, showing 10% lifetime risk.. Approximately 6% of cases can be attributed to an inherited genetic defect (mutation), while this proportion is about 12% for ovarian cancer. Besides breast and ovarian cancer, the susceptibility also includes, to a lesser extent, cancers of other organs. Inherited breast cancer should be suspected if the cancer develops at a markedly young age (below 40), if it affects both breasts, if it develops in a man, if the breast or ovarian cancer affects multiple family members in several generations. About half and one third of the mutations conferring susceptibility are located in the BRCA1 and BRCA2 gene, respectively. Carriers of a mutation in one of the two genes have a 40 to 80% risk of developing breast cancer, and 10 to 60% risk of developing ovarian cancer by the age of 75.

Indications for testing:

- bilateral breast cancer
- multiple primary breast cancer or breast AND ovarian cancer
- male breast cancer
- one of the above in a first-degree relative
- breast cancer developing below the age of 40
- one or several relatives with breast AND ovarian cancer within the same lineage
- relative with a confirmed mutation in the BRCA1 or BRCA2 gene

Method:

Amplification by PCR and bidirectional fluorescent sequencing of the exons or exon parts harbouring the mutation loci. The following 5 mutations are tested for: 185delAG, 300T>G, 5382insC (BRCA1), 6174delT, 9326insA (BRCA2).

Predictive value:

The tested mutations cover about 80% of all the mutations in the BRCA1 and BRCA2 genes, representing more than two thirds of all the inherited breast and ovarian cancer cases in the Caucasian population.

Sample requirement:

- buccal swab at room temperature *or*
2 ml blood in an EDTA (lavender top) tube, transported at +4 °C

*Lynch HT, et al.: Hereditary breast cancer: part I. Diagnosing hereditary breast cancer syndromes. Breast J. 2008 Jan-Feb;14(1):3-13. Review

**Fodor FH et al.: Frequency and carrier risk associated with common BRCA1 and BRCA2 mutations in Ashkenazi Jewish breast cancer patients. Am J Hum Genet. 1998 Jul;63(1):45-51.