

Hereditary breast cancer

Identity

Note hereditary or familiar form of breast cancer with a familiar background

Other names site-specific breast cancer

familiar breast-ovarian cancer

Inheritance follows an autosomal dominant pattern

5-10 % of all [breast cancers](#) have hereditary background

hereditary susceptibility for breast cancer has been counted to be 30-40 % of BRCA1 (see below, gene section), 10-30 % of BRCA2, less than 1 % of Tp 53, less than 1 % of PTEN and one third of unknown mutations; frequency of BRCA1 mutation is around 0.2 % in general population, 200 carriers among 100 000 individuals.

Clinics

Note hereditary breast cancer is a heterogenous entity including several clinical variants

Phenotype and clinics "site specific breast cancer" is characterized by the predominance of breast cancer, while "hereditary breast-ovarian cancer" has neoplasms in both organs

BRCA1 mutation carrier (chromosome 17q12-21) has early age at onset, and lifetime risk for breast cancer 50 % - 85 % and [ovarian cancer](#) 15 %-45 %; about 500 different mutations have been reported; possible increased risk of prostate cancer and [colon cancer](#)

BRCA2 (chromosome 13q12-13) mutation carrier has risk for breast cancer 30 %-85 %; about 300 different mutations have been reported; it is also associated for male breast cancer (6 %) and ovarian breast cancer (10% -20%); increased risk of prostate, laryngeal cancer and pancreatic cancer.

other genetic conditions associated with increased breast cancer risk are:

[Li-Fraumeni syndrome](#) (p53 mutation on chromosome 17p13) is characterized by very early onset of neoplasms, including [soft tissue sarcoma](#), [osteosarcoma](#), brain tumours, leukemia, [lung cancer](#), laryngeal cancer and adrenocortical cancer.; lifetime risk for cancer: about 90 % for women and 70 % for men

[Cowden syndrome](#) (PTEN, 10q23) is a rare type of autosomal dominant inherited condition of multiple hamartomas with increased risk of bilateral breast cancers and thyroid tumours

Muir-Torre Syndrome (MSH2 , [MLH1](#)), with also cancers of the gastro intestinal (GI)-tract, skin, genito urinary (Gu)-system

[Peutz-Jeghers Syndrome](#), with also abnormal melanin deposits, GI-polyposis, cancers of the GI-tract, uterus, ovary and testis.

[Ataxia-teleangiectasia](#) (linked to chromosome 11q21) autosomal recessive disorder with many clinical signs including increased risk for

breast cancer; homozygous AT carriers have around 100-fold risk of cancer

one third of familial breast cancers with hereditary background is still unknown; recent findings indicated that genotyping "BRCA3" locus at 13q and "BRCA2" locus at 2q may lead identifying the next mutations.

breast cancers of BRCA1 and, to lesser extent BRCA2 carriers differ from those of sporadic breast cancers: more high-grade tumours, pleomorphism, a higher mitotic count, less tubule formation, more often steroid receptor negative, DNA-aneuploid and more often higher s-phase fractions.

Treatment prophylactic bilateral mastectomy (reduces the risk of about 90 %) and/or ovarian ablation. Chemoprevention (antiestrogens, aromatase inhibitors, retinoids) mainly in clinical trials (tamoxifen may reduce the risk about 45 %).

early detection of cancers by screening mammograms (ultrasound) yearly, palpation, transvaginal ultrasound.

Prognosis prognosis is more dependent on extent of the disease at diagnosis than on the hereditary susceptibility

Genes involved and Proteins

Note see also [breast cancer](#)

Gene Name BRCA1

Location 17q21

DNA/RNA

Description 22 coding exons spanning over 70 kb of genomic DNA the BRCA1 mRNA has a size of 7.8 kb

Protein

Description the corresponding protein has 1863 amino acids, and 190-220 kDa

Expression wide

Function involved in DNA replication, repair transcriptional activation, cell cycle progression

Mutations

Germinal more than 500 sequence variations of the germline level have been reported

Gene Name BRCA2

Location 13q12-13

DNA/RNA

Description gene spanning more than 17 kb of genomic DNA; the coding sequence comprises 26 exons (10 254 nucleotides)

Protein

Description the corresponding protein has 3 418 amino acid residues (384 kDa)

Mutations

Germinal more than 300 unique germ-line mutations have been reported

Gene Name [P53](#)

Location 17p13

DNA/RNA

Description 11 exons

Protein

Function gene p53 encodes an ubiquitous nuclear protein involved in the control of genome integrity by preventing cells dividing before DNA damage is repaired

Gene Name [PTEN](#)

Location 10q23

DNA/RNA

Description 9 exons

Protein

Description the PTEN protein (also called MMA1) is an evolutionary conserved dual-extensive similarity with the cyto-skeletal protein tensin

Function tumour suppression since bi allelic inactivations, inactivating germline mutations are responsible for a cancer prone syndrome

Mutations

Germinal heterozygous germline mutations are responsible for the Cowden disease

Gene Name [LKB1](#)

Location 19p13

DNA/RNA

Description 10 exons spanning 23 kb

Protein

Description 433 amino acids

Expression wide

Function serine/threonine kinase; tumor suppressor gene

Homology heterozygous mutations are responsible for the Peutz-Jeghers syndrome

Gene Name [ATM](#)

Location 11q22-23

DNA/RNA

Description 66 exons spanning 184 kb

Protein

Description 3056 amino acids, 350 kDa

Function at the cell cycle checkpoint; induces G1 phase arrest

External links

[Orphanet](#) [Breast cancer, familial](#)

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