Breast Cancer 1 Gene

**Alternative Names**
- BRCA1
- Breast Cancer, Type 1
- Breast Cancer 1, Early-Onset
- Breast-Ovarian Cancer

**Record Category**
- Gene locus

**WHO-ICD**
N.B.: Classification not applicable to gene loci.

**Incidence per 100,000 Live Births**
N/A to gene loci

**OMIM Number**
113705

**Mode of Inheritance**
- Autosomal recessive

**Gene Map Locus**
17q21

**Description**
The BRCA1 protein is involved in DNA repair and mostly expressed in male and female genital organs and in breast. BRCA1 is highly expressed in cultured cells at the G1 phase in the presence of estradiol. However, the link between the sex hormone and breast cancer is indirect since BRCA1 does not have an estradiol receptor.

There are differences between the histopathology of breast cancers in carriers of BRCA1 and BRCA2 mutations. The findings can be interpreted as breast cancer due to BRCA1 has a different natural history from BRCA2 or apparently sporadic disease, which may have implications for screening and management.

Mutations in the BRCA1 gene were implicated as causes of different types of cancers including familial breast cancer, proliferative breast disease, ovarian cancer, papillary serous carcinoma of the peritoneum, and prostate cancer.

**Molecular Genetics**
A high percentage of familial breast cancers usually contain mutations in the BRCA1 and BARCA2 genes. The BRCA1 and BRCA2 genes are recessive tumor suppressor genes believed to be important for DNA repair. Abnormal BRCA1 and BRCA2 genes may account for up to 10% of all breast cancers. Women diagnosed with the BRCA1 or BRCA2 mutation develop breast and ovarian cancer with a lifelong likelihood of up to 85%. The presence of a mutation in any of these genes increases the risk for mutations to occur in other genes. That is why it is believed that the products of these genes act as repressors. The outcome of human BRCA1 or BRCA2 homozygotes is unknown and no case of human homozygosity has been documented despite extensive testing. Since the isolation of BRCA1 in 1994, more than 300 different germline mutations in BRCA1 gene have been identified.

**Epidemiology in the Arab World**
Rouba et al. (2000) investigated the extent of allelic imbalance at the BRCA1 region in Arabic women with breast cancer. They conducted DNA analysis in 13 cases and analyzed microsatellite markers D17S1323, D17S1325 and D17S855 intragenic to BRCA1. Microsatellite analyses showed 12 of 13 (92%) cases with loss of heterozygosity or microsatellite instability or both. This observation led Rouba and colleagues to the conclusion that the proportion of aberrant findings of the BRCA1 locus in breast cancer appears to be higher in Arabic women than in other populations. El-Harith et al. (2002) identified the unclassified BRCA1 variant Phe486Leu combined with Asn550His, and the unclassified BRCA2 variant Asp1420Tyr, in Arab
patients. Five BRCA1 polymorphisms and 6 BRCA2 polymorphisms were detected at different allele frequencies in both mutation carriers and patients with normal genotype. However, Denic et al. (2003) indicated that no single Arab woman with breast cancer was proven to be due to BRCA1 or BRCA2 mutation. They also suggested that the native population of the Gulf countries have one of the lowest incidences of breast cancer in the world.

**Egypt**

El-Harith et al. (2002) detected the BRCA1 disease-associated mutation Arg841Trp in an Arab patient from Egypt. The subject was diagnosed at 45 years of age and she is a mother of 4 children whom she lactated for approximately 2 years each.

**Iraq**

Bar-Saade et al., (1997) examined 639 unrelated healthy male and female Jews of Iraqi extraction and identified three individuals as 185delAG mutation carriers; thus, a carrier rate of 0.47%. Later, Bar-Saade et al. (1998) examined 43 unrelated women from Iraq for breast or ovarian cancer. They identified one patient with ovarian cancer as carrier for the 185delAG mutation in the BRCA1 gene.

**Jordan**

Atoum and Al-Kayed (2004) screened exons 2, 11, and 20 of the BRCA1 gene in 135 Jordanian breast cancer females. Of the studied patients 50 had a family history of breast cancer, 28 had a family history of cancer other than breast cancer, and 57 had no family history of any cancer. Five germline mutations were detected among breast cancer females with a family history of breast cancers (one in exon 2 and 4 mutations in exon 11). Another germline mutation (within exon 11) was detected among breast cancer females with family history of cancer other than breast cancer, and no mutation was detected among breast cancer females with no family history of any cancer or among normal control females.

**Morocco**

Bar-Saade et al. (1998) examined 17 unrelated women from Morocco for breast or ovarian cancer. They identified one patient with ovarian cancer as carrier for the 185delAG mutation in the BRCA1 gene. Bar-Saade et al. (1998) extended their analysis over DNA samples of 354 Jews of Moroccan origin, previously studied for Factor XI deficiency. They screened this group for the presence of the BRCA1 mutation 185delAG in the germline and detected it in four individuals (1.1%).

**Saudi Arabia**

El-Harith et al. (2002) concluded that BRCA1 and BRCA2 mutations are likely to contribute to the pathogenesis of familial breast cancer in female patients from the Kingdom of Saudi Arabia.

**Syria**

Bar-Saade et al. (1998) examined three unrelated Syrian women tested for breast or ovarian cancer. They identified one patient with breast cancer as carrier for the 185delAG mutation in the BRCA1 gene. Haplotype analysis in the patient revealed a unique pattern not available in other patients analyzed [See also: Yemen > Bar-Saade et al., 1998].

**Tunisia**

Mestiri et al. (2000) screened Tunisian women with familial or sporadic breast cancer for BRCA1 gene mutations using the Protein Truncation Test and DNA sequencing. A nonsense mutation was found in exon 11 of BRCA1 gene in a single case of familial breast cancer. DNA sequencing did not reveal any mutations in the other exons. The BRCA1 1294del140 mutation was found only in a patient with nonfamilial breast cancer. The 185delAG mutation was absent in all cases of breast cancer. Mestiri and colleagues suggested that the germline mutation of BRCA1 is implicated in breast cancer in Tunisia and that the 185delAG mutation is absent in Arab Tunisian women.

Charef-Hamza et al. (2005) studied the role of BRCA1 in sporadic breast cancer among Tunisian women. Tumors from 21 patients undergoing surgery for breast cancer were examined and none of them had a family history of the disease. The subjects were screened with a panel of three polymorphic microsatellite markers (D17S1322, D17S1323, and EDH-17B) within the BRCA1 region to identify patients for loss of heterozygosity (LOH) BRCA1 status. Microsatellite DNA analysis identified 13 of the 21 informative tumors displaying allelic loss in at least one marker, and yielding a relatively high frequency (61.9%) of LOH at the BRCA1 loci. Charef-Hamza et al. (2005) indicated that the high frequency of LOH at BRCA1 might reflect tumor aggressiveness among Tunisian women. The highest frequency of LOH (58.8%) was observed at D17S1322, whereas the frequency of allelic loss was lower for the other two markers: 35% at D17S1323, and 20% at EDH-17B. The study indicated that at least two target regions in the vicinity of BRCA1 were involved in LOH suggesting deletions of all or
part of the gene. There was no significant association between LOH in BRCA1 loci and tumor grade, therefore Charef-Hamza et al. (2005) concluded that deletions in the BRCA1 gene probably occurred early in sporadic mammary carcinogenesis among Tunisians.

United Arab Emirates
Denic and Al-Gazali (2002) examined the consequences of the long-term practice of consanguineous marriage on the prevalence of lethal cancer genes. They simulated, by computer, the mating of non-consanguineous and consanguineous populations over 40 generations. Denic and Al-Gazali proposed that in a randomly mating population, the BRCA1/2 carrier rate decreases on average 0.0035% every 25 years. Whereas in a highly consanguineous population, the carrier rate decreases on average 0.022% every 25 years, or six times faster than in a non-consanguineous population. The mechanism that better explains this result is that consanguineous couples see more of their homozygous offspring die before reaching reproductive age than do non-consanguineous couples. This is because humans homozygous for breast cancer mutations lack conserved tumor suppressor genes that perform essential cell functions and, thus, are expected to be biologically not viable (Denic and Gazali, 2002).

Yemen
Bar-Saade et al. (1998) examined nine unrelated women from Yemen for breast or ovarian cancer. They identified two patients with ovarian cancers as carriers for the 185delAG mutation in the BRCA1 gene. Haplotype analysis in one of the two patients revealed a unique pattern not available in other patients analyzed [See also: Syria > Bar-Saade et al., 1998]. Furthermore, Bar-Saade et al. (1998) extended their analysis over DNA samples of 200 Jews of Yemenite origin, previously studied for Factor XI deficiency, to screen for the presence of the BRCA1 mutation 185delAG in the germline. The mutation was not found in any of the Yemenite patient group. On the other hand, Lerer et al. (1998) uncovered one Jewish individual of Yemenite origin as carrier of the 5382insC mutation in BRCA1 [See also: Breast Cancer Gene 2 > Epidemiology in the Arab World > Yemen].

References


Related CTGA Records
Breast Cancer
Breast Cancer 2 Gene

External Links
http://www.breastcancer.org/
http://www.genetests.org/profiles/brcal
http://www.thebreastcancersite.com/cgi-bin/WebObjects/CTDSites

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