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Breast Cancer Genetics - An Overview

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Summary

Disease characteristics. Breast cancer is a malignant tumor of breast tissue suspected by clinical findings such as a breast lump, breast thickening, or skin change, or changes on mammography. Breast cancer is staged from 0 (earliest) to IV (most advanced) with survival being dependent upon the stage at diagnosis.

Diagnosis/testing. The diagnosis of breast cancer is established by histological examination of biopsied tissue. Inherited disorders in which breast cancer occurs can be recognized by the associated clinical findings (*e.g.*, Cowden syndrome, Bloom syndrome, Peutz-Jeghers syndrome, Werner syndrome, and xeroderma pigmentosum) or cancer history (*e.g.*, Li-Fraumeni syndrome). Inherited susceptibility to breast cancer may be identified through mutation analysis of the *BRCA1* gene or *BRCA2* gene. A *BRCA1* or *BRCA2* cancer-predisposing mutation is more likely to be present if the family history includes Ashkenazi Jewish ancestry, breast cancer diagnosed before age 50 years, bilateral breast cancer, ovarian cancer, or the occurrence of both breast cancer and ovarian cancer in the same person. Software is available for this risk calculation.

Genetic counseling. Breast cancer is considered to be a multifactorial disorder caused by both non-genetic and genetic factors. For individuals who do not have an underlying syndrome or a known inherited cancer susceptibility gene mutation, family history can be used to identify average-risk, moderate-risk, and high-risk individuals. Important aspects of family history include number of affected individuals, ratio of affected to unaffected relatives, closeness of biological relationship to affected relatives, ages at cancer diagnoses, presence of bilateral/multifocal breast cancer, presence of ovarian cancer, and case(s) of male breast cancer. The Claus model provides the best available estimate of risk based on family history of breast cancer. The Gail model projects individualized probabilities of developing breast cancer using some of the known non-genetic risk factors as well as limited family history information. Software based on the Gail model is available.

Definition

Breast cancer is a disease in which breast cells proliferate abnormally. The diagnosis of breast cancer is established histologically. Breast cancer may present as a breast lump, thickening, or skin change. Non-palpable cancers may be detected by mammography. A biopsy is necessary to confirm the diagnosis and determine the type of cancer present. When breast cancer cells metastasize from the original tumor and enter the blood stream or lymphatic system, they can form secondary tumors in other parts of the body. Bilateral cancer is diagnosed when separate primary breast cancers arise in each breast; multifocal breast cancer is diagnosed when breast cancer is present in more than one site in the same breast. Breast cancer is staged from 0 to IV, where 0 is a non-invasive tumor, Stage I is a small locally invasive tumor without lymph node involvement, Stage II is a medium-sized tumor with or without nodal metastases, Stage III cancer is a locally advanced cancer, usually with axillary node metastases, and Stage IV cancer has already metastasized to distant sites [Anderson and Moe 1996]. The survival rate is dependent upon the stage at which breast cancer is diagnosed.

Approximately 5% of benign breast biopsies reveal both excessive cell growth (hyperplasia) and cells that are abnormal (atypia). A diagnosis of atypical hyperplasia increases the risk for future breast cancer.

Prevalence

The National Cancer Institute (NCI) estimates that about 1 in 50 women will develop breast cancer by age 50 years and about one in ten women in the United States will develop breast cancer by age 80 years [Feuer et al 1993]. Excluding cancers of the skin, breast cancer is the most common cancer among women, accounting for one out of every three cancer diagnoses. In 1999, approximately 175,000 new cases of invasive breast cancer were expected to be diagnosed and 43,300 women were expected to die of the disease [ACS Breast Cancer Facts and Figures 1999-2000]. Male breast cancer is rare. The ratio of male: female breast cancer is 1 to 125.

Categories

Breast cancer is considered a multifactorial disorder caused by both non-genetic and genetic factors. A family history of breast cancer is an important contributor to breast cancer risk, as discussed below.

Non-genetic factors. Recognized contributors to breast cancer risk include menarche before age 12 years, menopause after age 55 years, first live birth after age 30 years, nulliparity, previous history of breast biopsies, atypical hyperplasia diagnosed by breast biopsy, obesity, alcohol use, hormone replacement therapy, and excessive radiation exposure. Most of these risk factors, with the exception of atypical hyperplasia, produce less than a twofold increase in risk of breast cancer and thus may contribute relatively little to risk in women from high-risk families. Other potential risk factors include a diet that is high in fat and low in fiber, fruits, and vegetables; lack of exercise; and induced abortion. The relationship between these risk factors and genetic predisposition is not yet understood. Some hormonal risk factors such as age of menarche and menopause could be influenced by polygenic inheritance.

Genetic factors. In addition to family history (see Risk Assessment), the following genetic factors are known to be associated with breast cancer risk:

- **Cancer susceptibility genes.** Major cancer susceptibility genes may account for 5-10% of breast cancer cases and may have a prevalence of 1/300 to 1/800 [Claus et al 1991, Peto et al 1996]. Two such genes, *BRCA1* and *BRCA2*, have been identified. These are described in BRCA1 and BRCA2 Hereditary Breast/Ovarian Cancer. However, there is evidence that other such genes exist [Serova et al 1997] and further discovery of such genes is an area of active research.

- **Genetic syndromes.** Less than 1% of all breast cancer is associated with the genetic syndromes: Cowden syndrome, Li-Fraumeni syndrome, Bloom syndrome, Peutz-Jeghers syndrome, Werner's syndrome, and xeroderma pigmentosum [Lindor and Greene 1998]. However, patients with these disorders may have a high breast cancer risk.

    - Cowden syndrome is an autosomal dominant cancer syndrome that includes breast cancer, thyroid cancer, and meningiomas. Diagnosis is established through identification of characteristic skin lesions (acral keratosis, facial trichilemmomas, and oral papules). Benign neoplasms of the breast and thyroid gland and hamartomatous polyps of the gastrointestinal tract are also seen. Mutations in the *PTEN* (*MMAC1*) gene (chromosomal locus 10q23) have been identified as a cause of Cowden syndrome [Liaw et al 1997].

    - Li-Fraumeni syndrome (LFS) is an autosomal dominant cancer syndrome that includes sarcomas, leukemia, and cancers of the brain, adrenal gland, and breast [Li et al 1988]. Approximately 50% of patients with Li-Fraumeni syndrome have identifiable mutations in the *TP53* gene (chromosomal locus 17p13) [Malkin et al 1990, Frebourg et al 1995]. The risk of developing breast cancer in an individual with a germline mutation in the *TP53* gene is approximately 49% by age 44 and 60% overall.

    - Other syndromes are described in detail elsewhere [Lindor and Greene 1998].

- **Common genetic variants**. Current research suggests a possible risk association between breast cancer and a number of common genetic variants. Further population-based studies will be needed to assess these genetic traits as contributors to multifactorial cancer risk. Such studies are likely to be an important area of research in the future. As the examples demonstrate, common genetic variants are likely to be considerably more common than high risk cancer-predisposing mutations, and as a result may have a larger effect on overall population risk. In addition, the effect of genetic variants of this kind is likely to vary with environmental exposures and other non-genetic risk factors.

    - Ataxia-telangiectasia (A-T) is a rare autosomal recessive disorder in which ataxia, oculocutaneous telangiectasia, immune deficiency, and increased susceptibility to childhood cancers occur. Epidemiological studies of families in which A-T has occurred suggest that women who are heterozygous for a mutation in the *ATM* gene may have a two- to fivefold higher risk for breast cancer than women from the general population [Swift et al 1991, Easton et al 1994]. Genetic studies have failed to identify a linkage between the *ATM* gene locus and familial breast cancer or to identify *ATM* mutations in patients with early-onset breast cancer [Fitzgerald et al 1997]. Such findings would not necessarily be expected if the breast cancer risk associated with the *ATM* gene is moderate and is mediated by environmental factors such as exposure to radiation, as has been proposed [Swift et al 1991].

    - N-acetyl transferase 2 (NAT2) is another potential risk factor that may interact with environmental exposures [Ambrosone et al 1996]. A case control study of women with and without breast cancer found that neither NAT2 status (i.e., whether or not the subject had an NAT2 variant that produced a rapid acetylation phenotype) nor smoking was independently associated with breast cancer risk. However, among slow acetylators who smoked, breast cancer risk was significantly increased [Ambrosone et al 1996].

    - A polymorphism in the *CYP17* gene may provide a protective effect. *CYP17* codes for a cytochrome P450 enzyme. In a population-based study, one polymorphism of this gene, when present in the homozygous state (A1/A1), was associated with late menarche and a reduced risk of advanced postmenopausal breast cancer (i.e., breast cancer with regional or metastatic spread) [Feigelson et al 1997]. The A1/A1 genotype was found in about one third of the study subjects and thus could have a significant impact on population risk.

    - Studies evaluating an association between glutathione transferase (GST) polymorphisms and breast cancer risk have produced conflicting results. Common polymorphisms in three GST genes (*GSTM1*, *GSTT1*, and *GSTP1*) have been described. Although other cancer risks have been found to be associated with these polymorphisms,

one study found no evidence of an associated breast cancer risk [Harries et al 1997]. However, a recent study utilizing prospective follow-up of subjects who had donated blood to a large research databank found evidence of increased breast cancer risk in women who were homozygous for a *GSTM1* polymorphism and a trend toward increased risk for carriers of polymorphisms in two other GST genes [Helzlsouer et al 1998].

Risk Assessment

The risk of an individual to develop breast cancer depends on the individual's family history and non-genetic risk factors. If the family history suggests autosomal dominant inheritance of breast or ovarian cancer risk, consideration is given to the use of *BRCA1* and/or *BRCA2* mutation analysis to evaluate risk status [Biesecker et al 1993, Peters 1994, Schneider et al 1994, Hoskins et al 1995]. Such testing should only be considered after pretest education and obtaining informed consent.

Methods to estimate an individual's risk for developing breast cancer have been developed, and studies to estimate the probability that an individual has a *BRCA1/BRCA2* cancer-predisposing mutation have been performed. Both the risk of developing breast cancer and the probability of having a *BRCA1/BRCA2* cancer-predisposing mutation depends to some extent on the family history of breast cancer.

Obtaining a Family History

When taking a family history to be used in estimating breast cancer risk, it is appropriate to obtain a history of all cancers in biological relatives, especially breast and ovarian cancers. For each cancer, the age of onset, laterality, mode of treatment, and any possible related prior environmental exposures should be noted, if possible. Medical records, including pathology reports, are useful to confirm the history of cancer in the patient and relatives. The following aspects of the family history can be used to identify average-risk, moderate-risk, and high-risk individuals:

- Number of affected relatives
- Ratio of affected to unaffected relatives
- Closeness of biological relationship of affected relatives
- Ages at cancer diagnoses
- Presence of bilateral/ multifocal breast cancer
- Presence of ovarian cancer
- Case(s) of male breast cancer

General Risk to Develop Breast Cancer Based on Family History

High risk. Women at high risk typically have multiple relatives with breast cancer diagnosed before 45-50 years of age, and one or more relatives affected with bilateral or multifocal breast cancer; they may also have a positive family history of ovarian cancer or male breast cancer [Hoskins et al 1995]. Inherited predisposition to cancer in these families may be the result of a highly penetrant autosomal dominant gene mutation, such as a cancer-predisposing *BRCA1* or *BRCA2* mutation.

Moderate risk. Women with a single affected first degree relative with cancer, or more distantly related family members with breast cancer, are usually at only moderately increased risk.

Average risk. Women with a first-degree relative diagnosed over the age of 60 years or two second-degree relatives diagnosed over the age of 50 years may have a risk indistinguishable from the average risk [Claus et al 1994].

Specific Risk to Develop Breast Cancer Based on Claus and Gail Models

The **Claus model** uses empiric data from the Cancer and Steroid Hormone Study and assumes that inherited risk is attributable to an autosomal dominant gene mutation with high penetrance [Claus et al 1991, Claus et al 1994]. The risk estimate is based on a woman's current age and the number of first and second degree relatives with breast cancer and their age of diagnosis. The Claus model provides the best available estimate of risk based on family history of breast cancer. The Claus model does not take into consideration any other factors known to increase breast cancer risk.

The **Gail model** [Gail et al 1989] projects individualized probabilities of developing breast cancer using some of the known non-genetic risk factors as well as limited family history information. It is based on the major predictors of risk identified in the Breast Cancer Detection Demonstration Project study: current age, age at menarche, age at first live birth, number of previous breast biopsies, presence of atypical hyperplasia, and number of first degree relatives (mother or sister) with breast cancer [Gail et al 1989]. The Gail model does not consider second degree relatives, paternal relatives, or ages of diagnosis of breast cancer. It provides a useful estimate of risk for women without a family history of breast cancer, but would be expected to overestimate risk in women whose mothers or sisters had breast cancer diagnosed at an elderly age and underestimate risk for women who have second and third degree relatives with early breast cancer. The Gail model has been validated as a predictor of breast cancer risk in women who adhere to regular mammography screening [Bondy et al 1994, Spiegelman et al 1994, Costantino et al 1999]. However, the validation studies indicate that the model overestimates risk in women who do not undergo routine screening [Bondy et al 1994, Spiegelman et al 1994]. The Gail model may overestimate risk by more than twofold among premenopausal women [Spiegelman et al 1994]. The Gail model is the basis for the Breast Cancer Risk Assessment Tool, a computer program that is available from the NCI. [Contact the National Cancer Institute Cancer Information Services at 1-800-4-CANCER to request the Breast Cancer Risk Disk.]

Probability of Having a *BRCA1/BRCA2* Cancer-Predisposing Mutation

Probability based on personal history of breast cancer. Several studies have looked at the probability of detecting a *BRCA1* cancer-predisposing mutation among women with a personal history of breast cancer, unselected for family history. In a population-based sample of women in western Washington State diagnosed with early-onset breast cancer, 6% of women diagnosed with breast cancer before age 35 years had a *BRCA1* cancer-predisposing mutation, and 7% of women diagnosed before age 45 years and with at least one first-degree relative with breast cancer had a cancer-predisposing *BRCA1* mutation [Malone et al 1998]. Among women in the state of North Carolina with breast cancer between the ages 20 and 74 years, about 3% of Caucasian women and 0% of African-American women had *BRCA1* cancer-predisposing mutations [Newman et al 1998]. A hospital-based study of women in the city of Boston found that 13% of women with breast cancer diagnosed before age 30 years had a cancer-predisposing *BRCA1* mutation and 21% of Ashkenazi Jewish women with breast cancer diagnosed before age 40 years had the 185delAG mutation in *BRCA1* [Fitzgerald et al 1996].

Probability based on family history. Initial studies estimated that 50% of families with inherited breast cancer [Szabo and King 1995] and approximately 75% of families with inherited breast and ovarian cancer [Narod et al 1995] had a cancer-predisposing *BRCA1* mutation. From initial studies, *BRCA2* cancer-predisposing mutations were estimated to occur in approximately 15-30% of families with inherited breast cancer [Szabo and King 1995] and an unknown proportion of families with inherited breast and ovarian cancer [Narod et al 1995]. Subsequent clinical studies have identified cancer-predisposing mutations less frequently. These differences may reflect the criteria used to define a high-risk family and the sensitivity of molecular methods currently available, i.e., even families linked to *BRCA1* or *BRCA2* may not be found to have an identifiable mutation.

Subsequent studies have further attempted to determine the probability of a cancer-predisposing mutation among families with multiple cases of breast and/or ovarian cancer. In a multi-center study, women were referred for *BRCA1* and *BRCA2* mutation analysis if they had been diagnosed with breast cancer before age 50 years or ovarian cancer at any age and also had at least one first or second-degree relative with either diagnosis. Among this selected group, the likelihood of the proband having a *BRCA1* or *BRCA2* cancer-predisposing mutation was over 50% if she had breast cancer diagnosed before age 50 years and three or more of the following: bilateral breast cancer or ovarian cancer, a diagnosis of breast cancer before age 40 years, a relative with breast cancer diagnosed before age 50 years, or a relative with ovarian cancer [Frank et al 1998]. A referral clinic in the state of Pennsylvania found cancer-predisposing *BRCA1* mutations in 40% of families with breast and ovarian cancer but in only 7% of families with breast cancer only [Couch et al 1997]. Ashkenazi Jewish ancestry also increased the likelihood of finding a cancer-predisposing mutation [Couch et al 1997, Frank et al 1998]. In a referral clinic in Germany, families were evaluated for *BRCA1* mutations if there were three or more members with breast or ovarian cancer, with at least two affected before age 60 years. A cancer-predisposing mutation was found in 33% of the families with both breast and ovarian cancer and in 17% of families with breast cancer only [Chang-Claude et al 1998].

Calculation of probability. Taken together, these studies indicate that a *BRCA1* or *BRCA2* cancer-predisposing mutation is more likely to be present if the family history includes Ashkenazi Jewish ancestry, breast cancer diagnosed before age 50 years, bilateral breast cancer, ovarian cancer, or the occurrence of both breast cancer and ovarian cancer in the same person [Couch et al 1997, Shattuck-Eidens et al 1997, Chang-Claude et al 1998, Frank et al 1998, Parmigiani et al 1998]. Because these studies were based on referral populations, the quantitative estimates of mutation frequency cannot necessarily be generalized to patients seen in primary care settings.

A method of calculating the probability of the presence of a cancer-predisposing *BRCA1* or *BRCA2* mutation has been developed. This calculation is based on observations in referral populations in which the majority of women tested were affected with cancer [Berry et al 1997, Parmigiani et al 1998]. Software is available.

Genetic Testing

Pre-Test Education and Counseling

The importance of providing education and obtaining informed consent prior to performing testing for cancer-predisposing gene mutations has been emphasized by several expert groups [ASCO 1996, McKinnon et al 1997, Geller et al 1997].

Pre-test education for patients includes discussion of the following suggested components:

- The patient's motivation for requesting testing and preconceived beliefs about the test
- The patient's perceptions of his/her risk of developing cancer
- The patient's readiness for testing and optimal timing for testing
- Alternatives to testing, such as DNA banking GENETests
- Inability of genetic testing to detect the presence or absence of cancer
- The patient's and family's support systems, and possible need for additional psychological support
- The patient's need for privacy and autonomy
- The possible effects of positive, negative, or uninformative test results on:
  - Risk for cancer in individuals who have a cancer-predisposing mutation: detailed in BRCA1 and BRCA2 Hereditary Breast/Ovarian Cancer
  - Patient's utilization of cancer screening protocols
  - Risk status for other family members: *BRCA1* and *BRCA2* cancer-predisposing mutations are inherited in an autosomal dominant manner. Each child of an individual with a cancer-predisposing mutation in the *BRCA1* or *BRCA2* gene has a 50% risk of inheriting the cancer-predisposing mutation.
  - Insurance coverage and employment: An individual found to have an inherited susceptibility to cancer could face discrimination in access to health insurance and employment.
  - Patient's emotional status: depression/anxiety/guilt

- Relationships with partner, children, extended family, friends

It is important to note that prenatal testing and testing of at-risk children under the age of 18 years are not typically available.

Molecular Genetic Testing

Laboratory technique. Molecular genetic testing for *BRCA1* and *BRCA2* cancer-predisposing mutations is now offered both as a clinical service and within research protocols (see BRCA1 and BRCA2 Hereditary Breast/Ovarian Cancer). The specific DNA-based testing techniques performed by various laboratories may include: allele specific oligonucleotide (ASO) testing, protein truncation testing (PTT), conformation sensitive gel electrophoresis (CSGE) [Ganguly et al 1993], single stranded conformational polymorphism (SSCP), complete sequencing, Southern blot analysis, or a combination of these and/or other techniques. It is important to note that no currently available technique can guarantee the identification of all cancer-predisposing mutations in the *BRCA1* or *BRCA2* genes [Ford et al 1998]. Clinical testing information: BRCA1 GENETests BRCA2 GENETests

Sensitivity. The sensitivity of tests for detecting *BRCA1* or *BRCA2* cancer-predisposing mutations is dependent on the method used for DNA analysis and the a priori risk of the person tested to have a mutation in either gene based on the person's cancer history, family history, and ethnic background.

Testing strategy in a family. It is strongly recommended that the genetic test be offered to an affected individual prior to offering it to at-risk unaffected family members. Testing an affected individual is the most effective way of determining if a *BRCA1* or *BRCA2* mutation is causative of breast cancer within a family. After a cancer-predisposing mutation has been identified in an affected family member, *BRCA1* or *BRCA2* mutational analysis is more informative for unaffected relatives.

Interpretation of positive test results for mutations of uncertain clinical significance. When full gene sequencing is the method used for testing, mutations of uncertain clinical significance may be identified, such as previously undescribed missense mutations that are not predicted to result in a loss of protein function. Such alterations present a dilemma for physicians who are making patient management decisions. Three methods are available to determine the clinical significance of these mutations: 1) family studies to determine whether the mutation segregates with cancer in family members (which is the most practical and clinically useful method); 2) allele frequency analysis to determine whether the allele has a higher frequency in cancer patients than in the general population; and 3) protein function assays to measure the effect of the mutation on the protein [Shattuck-Eidens et al 1997]. Since these approaches are difficult to implement and usually not feasible as part of a clinical study, the clinical significance of these ambiguous mutations may remain unclear indefinitely.

Interpretation of negative test results.

- When a cancer-predisposing *BRCA1* or *BRCA2* mutation cannot be identified in an affected individual from a family with an increased risk of an inherited predisposition to breast cancer, negative results are uninformative, and the possibility of a false negative test must be considered [Geller et al 1997]; thus, the affected individual may still have an inherited cancer-predisposing mutation in the *BRCA1* or *BRCA2* gene. She may also have a mutation in some other gene that predisposes to breast cancer.

- If the affected family member has no identifiable *BRCA1* or *BRCA2* cancer-predisposing mutation or is unavailable for testing, all negative *BRCA1* and *BRCA2* test results in other family members must be considered uninformative.

- An at-risk relative who does not have the *BRCA1* or *BRCA2* cancer-predisposing mutation identified in an affected family member is considered to have a true negative result. It is appropriate to advise the individual that a negative result does not reduce her cancer risk below that of the general population. Furthermore, if that person is from a high-risk ethnic group, *e.g.*, of Ashkenazi Jewish descent, it may be prudent to test for all the cancer-predisposing mutations known to be common in that population, even if a single cancer-predisposing mutation has already been identified in an affected family member.

Management

Although a number of interventions have been postulated to reduce the morbidity and mortality from breast cancer in women with confirmed *BRCA1* or *BRCA2* cancer-predisposing mutations [Burke et al 1997], there are no interventions of proven benefit for individuals with a genetic susceptibility to breast or ovarian cancer beyond the routine mammography screening recommended to women of average risk beginning at age 40 or 50 (see NCI Guidelines, Cancernet). Additional recommendations are made on the basis of presumptive benefit.

Resources

GeneClinics provides information about selected national organizations and resources for the benefit of the reader. GeneClinics is not responsible for information provided by other organizations. —ED.

- **American Cancer Society**
  Provides contact information for regional support groups and programs, cancer information, patient and family education materials, and free mammograms
  1599 Clifton Rd NE
  Atlanta, GA 30329

Phone: 800-227-2345
www.cancer.org

- **Breast Cancer Information Core NHGRI (National Human Genome Research Institute) Cancer Genetics Branch**
  www.nhgri.nih.gov/Intramural_research/Lab_transfer/Bic

- **Cancernet**
  cancernet.nci.nih.gov
  Genetics, Causes, Risk Factors, Prevention of Breast Cancer: cancernet.nci.nih.gov/cancer_types/breast_cancer.shtml#genetics

- **CancerCare**
  275 7th Avenue
  New York, NY 10001
  Phone: 212-302-2400; 1-800-813-HOPE (4673)
  Fax: 212-719-0263
  Email: info@cancercare.org
  www.cancercare.org

- **Facing Our Risk of Cancer Empowered (FORCE)**
  A discussion forum specifically for women who are at a high risk of developing ovarian cancer or breast cancer.
  934 N University Dr, PMB #213
  Coral Springs, FL 33071
  Phone: 954-255-8732
  Email: info@facingourrisk.org
  www.facingourrisk.org

- **Genetics of Breast and Ovarian Cancer (PDQ)**
  CancerNet - A service of the National Cancer Institute
  cancernet - genetics of breast and ovarian cancer

- **Gilda's Club**
  195 W Houston St
  New York, NY 10014
  Phone: 212-647-9700
  Fax: 212-647-1151
  www.gildasclub.org

- **Lifetime Probability of Breast Cancer in American Women**
  www.meb.uni-bonn.de/cancernet/600056.html

- **The National Alliance of Breast Cancer Organizations**
  An advocacy group that serves as an umbrella for 370 breast cancer groups nationwide. Provides information, a newsletter, and treatment information. Also provides grants for programs on early detection and education.
  9 East 37th Street, 10th Floor
  New York, NY 10016
  Phone: 212-889-0606; 888-806-2226
  Email: NABCOinfo@aol.com
  www.nabco.org

- **National Breast Cancer Centre Home Page -Australia**
  www.nbcc.org.au

- **The National Breast Cancer Coalition**
  An advocacy group seeking public policy change to benefit breast cancer patients and survivors.
  1701 L St NW, Suite 1060
  Washington DC 20036
  Phone: 202-296-7477; 800-935-0434

- **NCBI Genes and Disease Webpage**
  www.ncbi.nlm.nih.gov/disease/Breast-ovary.html

- **National Cancer Institute**
  www.nci.nih.gov

- **The National Coalition for Cancer Survivorship**
  A consumer organization that advocates on behalf of all people with cancer.
  1010 Wayne Avenue, Suite 770
  Silver Spring, MD 20910
  Phone: 877-NCCS-YES (877-622-7937)
  Fax: 301-565-9670

Email: info@cansearch.org
www.cansearch.org

- **Ovarian Cancer** (National Ovarian Cancer Coalition)
www.ovarian.org

- **Susan G Komen Breast Cancer Foundation**
Information, referrals to treatment centers. Answers questions from recently diagnosed women and provides emotional support. Funds research and programs for women who do not have adequate medical service and support.
Occidental tower
5005 LBJ Freeway, Suite 370 LB74
Dallas, TX 75244
Phone: 800-462-9273 (hotline); 214-450-1777
Email: helpline@komen.org
www.breastcancerinfo.com

- **Y-Me National Organization for Breast Cancer Information**
Hotline staffed by counselors and volunteers who have had breast cancer. Information, referrals, support.
212 West Van Buren St, 5th Floor
Chicago, IL 60607
Phone: 800-221-2141
Fax: 312-294-8597
www.y-me.org

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