Genetic Counseling and Testing in Breast Cancer

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Cancer is always genetic, but rarely inherited

- Usually arises sporadically from mutations in multiple genes controlling or influencing cell division—tumor suppressors, oncogenes

- ~5-10% of most cancers are hereditary—caused by germline inheritance of high risk cancer predisposing gene mutation
Cancer can be hereditary, familial, or sporadic.

- **Sporadic Cancer**: 65%
- **Familial Cancer**: 15-25%
- **Hereditary Cancer**: 5-10%

Understanding which category your cancer falls into will help guide the management of your risk better.
Patients with a Personal History of Cancer

- Up to 22% of breast cancer patients have personal or family history risk factors that make them appropriate for Hereditary Breast and Ovarian Cancer syndrome evaluation.

- 100% of patients diagnosed with epithelial ovarian/fallopian tube/primary peritoneal cancer meet criteria for Hereditary Breast and Ovarian Cancer syndrome testing.
Hereditary Breast Cancer

Most often associated with a mutation in the BRCA1 or BRCA2 gene

Several other breast cancer risk genes are known, such as CHEK2, ATM, PALB2, PTEN, CDH1, TP53

Additional breast cancer risk genes will be discovered
“Red Flags” for HBC/HBOC

- Breast cancer diagnosed at or before age 50 (includes invasive and DCIS)
- Ovarian/fallopian tube/primary peritoneal cancer at any age
- Male breast cancer at any age
- Multiple primary cancers (2 separate breast cancers/breast and ovarian cancer)
- Ashkenazi Jewish ancestry
- Multiple relatives with breast and/or ovarian cancer
- Other factors: triple negative breast ca, family hx of pancreatic ca, prostate ca, melanoma, sarcomas, brain tumors, some other cancers
- BRCA or other known cancer susceptibility gene mutation in family
Genetic Testing Is a Process

- Pretesting evaluation, education, genetic counseling, and informed consent
- Laboratory analysis
- Interpretation of results
- Follow-up: support, education, and medical management
PANEL TESTING

• Can evaluate several different genes at the same time
• Many different panel test options available
• Likelihood of detecting one or more variants of uncertain significance is greater than in single gene testing
• May detect pathogenic variant in gene for which well established medical management guidelines are not yet known
A PANEL APPROACH MAY CHANGE MEDICAL MANAGEMENT

even if it includes genes not associated with breast cancer

3.1% Other high-risk genes associated with breast cancer (PTEN, TP53, CDH1, and STK11)

10.3% Genes not associated with breast cancer (MLH1, MSH2, MSH6, PMS2, EPCAM, APC, MUTYH, CDKN2A, RAD51D, RAD51C, and SMAD4)

48.7% Hereditary breast and ovarian cancer syndrome-specific genes (BRCA1 and BRCA2)

37.9% Moderate-risk genes associated with breast cancer (PALB2, CHEK2, ATM, BRIP1*, BARD1, and NBN)

MUTATIONS IDENTIFIED BY A 25 GENE CANCER PANEL
in patients with a personal history of breast cancer

*Evolving data suggests that BRIP1 may not be associated with significantly increased breast cancer risk.
Benefits and Limitations

• **Benefits**
  - Provides risk information for individuals and families
  - Allows early detection and risk reducing strategies
  - May alleviate uncertainty and relieve anxiety

• **Limitations**
  - Not all mutations are detectable
  - Negative result is fully informative only if a deleterious mutation has been identified in the family
  - Some genetic variants are of unknown clinical significance
WHAT DO WE HAVE TO OFFER?

• EARLIER AND MORE FREQUENT SCREENING

• CHEMOPREVENTION

• RISK REDUCING SURGERY
Why is this important?

• To help determine who **IS** at increased risk
  – Routine screening is **not** sufficient
  – Quality and duration of life can be improved
• May impact cancer treatment
• To identify who is **NOT** at increased risk
  – Relieve anxiety
  – Standard screening is appropriate
Health Insurance Discrimination?

Health insurance discrimination is NOT a significant risk

Being unaware of mutation status/increased cancer risk IS!
DNA BANKING

COST $100 FOR 20 YEAR STORAGE

CAN BE EXTENDED AS NEED BE

PRIVATE OWNERSHIP
Knowledge is Power.

And Hope.