When to Refer for Genetic Counseling

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Personal Risk for Cancer

- Environmental Factors
- Lifestyle
- Genetic Factors
- Biologic Aging
All Cancers Have Genetic Origins

- Somatic Mutations
  - Occur in non-germline tissues (breast, colon, lung, blood cells, etc.)
  - NOT inherited
- Sporadic cancer

- Germline Mutations
  - Mutation is in all cells of the body
  - Occur initially in eggs and sperm
- Hereditary Cancer Syndromes
Most Cancer is Sporadic

- Sporadic: 60%
- Familial: 30%
- Hereditary: 10%
Hereditary

Br 35
Br 40
Br 48

Br 38
NCCN Guidelines for Genetic Referral

- Breast cancer <= 50 years of age
- Triple negative breast cancer
- Two primary breast cancers
- Two or more family members with breast cancer
- Ovarian cancer at any age
- All male breast cancers
- Breast cancer at any age in an individual with Ashkenazi Jewish ancestry.
BRCA1 and BRCA2 Genes

- Hereditary Breast and Ovarian Cancer Syndrome
- 50% - 87% risk for breast cancer.
- 20% - 40% risk for ovarian cancer.
- Increase risk for melanoma, pancreatic and prostate cancer.
High Risk Genes

- **PTEN** – Cowden Syndrome
  - Breast, thyroid, endometrial cancers
- **TP53** – LiFraumeni Syndrome
  - Breast, sarcoma, brain, adrenal gland cancers
- **CDH1** – Hereditary Diffuse Gastric Cancer and Lobular Breast Cancer
  - Breast and gastric cancer
- **STK11** – Peutz-Jegher Syndrome
  - Breast, colon, gastric, ovarian, pancreatic cancers
Traditional vs. NextGen Sequencing

**SANGER SEQUENCING:**

1 SEQUENCE READ PER BP

**NGS:**

MULTIPLE SEQUENCE READS PER BP

Slide created by Kelly Gonzalez, MS, CGC, Ambry Genetics
Panels/Multi-Gene Testing

- Next Generation Sequencing (NGS) panels starts to be offered clinically in March 2012.
- Unable to include BRCA1 and BRCA2
- Number of genes now available on panels:
  - Breast Cancer - 18 genes
  - Colon Cancer - 16 genes
  - Ovarian Cancer - 23 genes
  - Pancreatic Cancer – 16 genes
  - All Cancer - 29 genes
In June 2013...

- Supreme Court rules human genes cannot be patented.
- Myriad Genetic Laboratories no longer the only lab to offer testing for the BRCA1 and BRCA2 genes.
- Panel testing starts to be used more often.
### Additional Breast Cancer Genes

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<thead>
<tr>
<th>High Risk Genes</th>
<th>Moderate Risk</th>
<th>Unknown Risk</th>
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<td>PTEN</td>
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NCCN Guidelines - Multi-Gene Testing

- General overview with examples
- Points in favor
- Limitations in use
- Issues to consider for less characterized genes
- General Recommendations
  - Because of their complexity hereditary cancer multigene tests should be ordered in consultation with a cancer genetics professional.
- Laboratory considerations
Benefits

- **Ability to look at several genes at one time**
  - Patients who do not meet specific criteria
  - Cost- and time-effective

- **Higher mutation detection rate**
  - 17% of BRCA-negative, high-risk breast cancer families will have a gene identified on panel.

- Clarify risk

- Offer medical management guidance
Challenges

- Limited data on cancer risk for some genes.
  - Management?
- How to interpret results for family members?
  - Do you test family members?
- Mutations for unrelated cancer risk
- Risk for non-cancer related diseases
- Increase turnaround time
- Informed consent
- Increase likelihood of Variant of Uncertain Significant
Result Interpretation

Medical management based on personal and family history. Uncertain results do not influence recommendations for care.

Medical management based on cancer risks linked with gene where mutation found.
Decline in Rate of BRCA1/2 Variants of Uncertain Significance

Eggington et. al. Current Variant of Uncertain Significance Rates in BRCA1/2 and Lynch Syndrome Testing (MLH1, MSH2, MSH6, PMS2, EPCAM), March 2012, ACMG Poster Presentation.
Laboratories

- Panels differ
  - Different high risk panel depending on lab used.
- Gene coverage differs
- Classification of variants of uncertain significance
- Data sharing
  - Facilitates variant classification
Genetic Counseling

- Discuss testing available
- What testing is recommended
- What information does the patient want
- When does the patient need the information
- Possible results
Medical Management

- Increased surveillance
  - Breast mammogram
  - Breast MRI

- Prevention
  - Preventive surgeries
    - Mastectomy
    - Removal of the ovaries
  - Chemoprevention
    - Tamoxifen (reduces breast cancer risk)
    - Birth control pills (reduce ovarian cancer risk)
You don’t need to know everything. You do need to know when it’s time to refer.