Genetics 101 for the Ovarian Cancer Patient

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Basic Genetics
Chromosomes
How Cancer Forms

**Sporadic cancer**

Normal Cell → Loss of Proper Growth Control → Tumor Develops

**Hereditary cancer**

Predisposed Cell → Loss of Proper Growth Control → Tumor Develops
Basics of Cancer
Origin Cancer

Sporadic (70%)
- Cancer occurs by chance or related to environmental factors
Sporadic Cancer

Ovarian, 60
Origin Cancer

Hereditary (18%)
- Gene Mutation is inherited in family
- Significantly increased cancer risk
Origin Cancer

Familial (12%)
- Multiple Genes and Environmental Factors
- Some increased cancer risk
Indications of an Inherited Cancer Family

- Early age at diagnosis
- Multiple primary cancers or bilateral cancers
- Multiple family members affected with the same cancer or related cancers
- Multiple generations affected with cancer
- Rare cancers (i.e. male breast cancer)
- Clustering of certain cancers within a family (i.e. breast/ovarian, colorectal/endometrial, breast/pancreatic)
- Ashkenazi Jewish ancestry
Ovarian Cancer Genes

- **BRCA1**: ~70%
- **BRCA2**: ~20%
- Lynch: ~2%
- Other genes: ~8%

18%
Why it matters to you..
Breast Cancer Risk

- General Population
- Moderate Risk
- BRCA2
- BRCA1
Therapy Decisions

• PARP inhibitors
  o December 2016- rucaparib (Rubraca) approved for BRCA-positive patients who have received at least two prior lines of chemotherapy

  o 2017- olaparib (Lynparza) approved for BRCA-positive patients who have received at least three prior lines of chemotherapy

Aim 2: Four clinic trials with novel drug combinations to extend PARP inhibitor use
Other Cancers

- Pancreatic
- Melanoma
- TBD
Why it matters to your family..
Ovarian Cancer Risk

General Population  FDR w/ Ovarian Ca  BRCA2  BRCA1
BRCA Cancer Risk in Men

- Male Breast Cancer
  - Up to 7% lifetime risk

- Prostate Cancer
  - Elevated risk
Should you do the test...
Yes if.. 

... 

It will benefit you 

Or 

Its will benefit your family
What test should you do...
Types Of Test

• Panel Testing
  OR
• BRCA Only

BRCA1 9.5%
BRCA2 5.1%
Other OC gene 4%
No mutation 80%

(Walsh et al, PNAS, 2011)
# Panel Testing

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Limitation</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify source of cancer risk in your family</td>
<td>Not all mutations are found</td>
<td>Anxiety and worry</td>
</tr>
<tr>
<td>Identify your additional cancer risk</td>
<td>Limited data for some genes</td>
<td>Frustration by lack of data</td>
</tr>
<tr>
<td>Future knowledge</td>
<td>May not explain your cancer risk</td>
<td>Confusion</td>
</tr>
<tr>
<td></td>
<td>Lack of clear medical recommendation</td>
<td>Potential negative impact on life insurance</td>
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Next generation genetic testing

TARGET Population:
- Women without ovarian cancer
- Age ≥30
- No prior genetic testing

GOAL
Assess how well we can deliver genetic testing for breast and ovarian cancer risk to women in their living room

Making genetic testing accessible

The study of genetic testing from your living room.
A Stand Up to Cancer/SU2C initiative at MD Anderson
Possible Results

• No mutation identified

• Mutation identified in a gene associated with ovarian cancer

• Mutation identified in a gene not associated with ovarian cancer

• Variant of uncertain significance (VUS)
Ovarian Cancer Gene Identified

Now What??
Risk Management

- Increased Surveillance
- Chemo-prevention
- Preventive Surgery
## Surveillance and Screening for Women

<table>
<thead>
<tr>
<th>Breast</th>
<th>Clinical breast exam</th>
<th>Once-twice a year starting at age 25</th>
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<tbody>
<tr>
<td></td>
<td>MRI</td>
<td>Once a year starting at age 25</td>
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<tr>
<td></td>
<td>Mammogram</td>
<td>Once a year starting at age 30</td>
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<tr>
<td>Ovarian</td>
<td>Pelvic exam</td>
<td>May be considered</td>
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<tr>
<td></td>
<td>Transvaginal</td>
<td></td>
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<tr>
<td></td>
<td>ultrasound</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CA-125 blood test</td>
<td></td>
</tr>
<tr>
<td>Risk Reducing Options for Women</td>
<td></td>
<td></td>
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<tr>
<td>--------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Breast</strong></td>
<td><strong>Chemoprevention</strong></td>
<td>% Risk Reduction</td>
</tr>
<tr>
<td></td>
<td>• Tamoxifen for 5 years</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td><strong>Option of Surgery</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Prophylactic mastectomy</td>
<td>90-95%</td>
</tr>
<tr>
<td></td>
<td>• Prophylactic oophorectomy</td>
<td>50% (premenopausal)</td>
</tr>
<tr>
<td><strong>Ovarian</strong></td>
<td><strong>Chemoprevention</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Oral contraceptives for 5 yr</td>
<td>50-60%</td>
</tr>
<tr>
<td></td>
<td><strong>Option of Surgery</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Prophylactic oophorectomy</td>
<td>96%</td>
</tr>
</tbody>
</table>
Next generation prevention

**GENETIC MUTATION**
- BRCA1
- BRCA1
- BRIP1
- PALB2
- RAD51C
- RAD51D
- BARD1
- MSH2
- MSH6
- MLH1
- PMS2

Removal of Tubes & Ovaries

Removal of Tubes Now

Removal of Ovaries Later

Menopause Symptoms/Sexual Function

**Women Choosing Surgical Prevention**

WISP Clinical Trial

NCT:01907789
Quiz
What additional info do you want?

Helen Palmquist
Stage IIIc epithelial ovarian cancer
Age 41
What else do you want to know?

**Brother**
Prostate Cancer
Age 55
(diagnosed just a few months before Helen)

**Father**
Pancreatic Cancer
Age 77
What do you recommend?
What do you recommend now?

⇒ = BRCA 2 positive
Cancer Prevention

- Daughter - Negative
  - Son - Positive
- Daughter - Negative
  - Son - Positive
- Son - Positive
- Daughter - Negative
  - Son - Positive
  - PGD
  - Daughter - Negative
  - Son - Negative
  - Daughter - Negative
Questions & Conversations

Helen S. Palmquist
Iris Romero, MD
• **Iris Romero, MD**
  - Gynecologic Cancer Prevention Clinic
  - 773-702-6722
  - [http://www.uchospitals.edu/physicians/iris-romero.html](http://www.uchospitals.edu/physicians/iris-romero.html)

• **Comprehensive Cancer Risk Clinic**
  - 1-855-702-8222

• **Clinical Trial: Stand Up 2 Cancer Women Choosing Surgical Intervention**
  - Morgan Whipkey
  - 773-702-3972