Molecular Management of Cancer Genetics

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Undergraduate Research Day
Outline

- Motivation for Molecular Data Collection
- Examples of Specific Genes Correlating with Cancer Development
- Usefulness of Cancer Panels

Clinical Genomics to Improve Treatment
  - Traditional Tumor Markers
  - Expression Profiling
  - Targeted Breast Cancer Treatments
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Motivation for Molecular Data Collection

Motivating Reasons:
- Familial Inherited Disorders
- Family Ancestry
- Family Planning
- Personal Curiosity
- Cultural Susceptibility

Considerations on the effects of these genetic test results.

✧ Prophylactic treatments (ex: PBM-prophylactic bilateral mastectomy)
✧ Earlier screenings (ex: mammogram)
✧ Increased blood work and physicals
Specific Genes and Cancer Development

Examples of high-penetrance genes that a single-gene test may detect:

- **BRCA 1 and BRCA 2**
  - 12% population risk
  - 55-65% risk if mutant BRCA
  - 39% ovarian cancer risk
    (BRCA 1)

- **P53**
  - “Guardian of the genome”
  - 50% of all cancers
  - Li-Fraumeni Syndrome

- **APC**
  - Familial Adenomatous Polyposis
Cancer Panels

Benefits:
- Increased sensitivity
- Increased target audiences
- Better risk assessment
- Improved clinical decisions

Challenges:
- Increased complexity of test results
- VUS
- Estimating risk
- Effective patient communication
## Breast Cancer Gene Panels and Assays

<table>
<thead>
<tr>
<th>Test:</th>
<th>Company</th>
<th>Who is eligible?</th>
<th>Number of genes tested:</th>
<th>Goal of Test:</th>
<th>FDA Approved:</th>
</tr>
</thead>
</table>
| **OncoType DX - Breast** | Oncotype DX              | - Stage I or II breast cancer  
- Invasive  
- Estrogen-receptor positive  
- Node-negative  
- Diagnosed with DCIS (ductal carcinoma in situ) | 21                      | - Recurrence risk  
- Benefit from chemotherapy  
- Benefit from radiation therapy if treated for DCIS | Approved       |
| **Mammaprint** | Agendia                  | - Stage I or II breast cancer  
- Invasive  
- <5cm tumor estrogren receptor positive or negative | 70                      | - Recurrence after 10 years | Approved       |
| **Mammostrat** | Clariant Diagnostic Services | - Stage I or II breast cancer  
- hormone-receptor positive | 5                       | - Recurrent risk | Not Approved |
| Breast Cancer Prognostic Gene Signature Assay (PAM50) | cancer with node-negative  
-Stage II with 1-3 nodes-positive  
-Hormone-receptor positive  
-Invasive  
-Post-surgery and hormone therapy patient | 5-10 years  
-Benefits of hormone therapy after 5 additional years in postmenopausal women |
|-----------------------------------------------------|---------------------------------------------------------------|
| **EndoPredict**  
**Sividon Diagnostics (distributed by Myriad)** | -Stage I or II breast cancer  
-Hormone-receptor positive  
-HER-2 negative  
-Node-negative  
-3 or more nodes-positive | **12**  
-Chance of metastasis after 10 years of diagnosis | Not approved |
| **Breast Cancer Index**  
**bioTheranostics** | -Early-stage breast cancer (stage I-III)  
-Node-Negative  
-Hormone-receptor positive | **7**  
-Recurrence after 5-10 years  
-Benefits of hormone therapy | Not approved |
Clinical Genomics

Traditional Tumor Markers

- Antigens, hormones, glycoproteins, immunoglobulins, gene expression changes
- Example: Prostate Specific Antigen (PSA)
- CANNOT solely be diagnostic

Expression Profiling

- Identifying cell RNA activity
- RT-PCR, microarray technology, FISH, etc.
Clinical Genomics in Breast Cancer

- Oncotype Dx Breast
- TAILORx Trial
- qRT-PCR
- 21 genes tested

- Mammaprint
- MINDACT Trial
- Microarray
- 70 genes tested
Targeted Breast Cancer Treatments

- HER2 receptor status
- Estrogen and progesterone receptor status
- Results of Breast Cancer Assay
  - Chemotherapy versus hormone therapy only
- CYP2D6 enzyme expression
  - Major enzyme in Tamoxifen catabolism