Genetics in Cancer Treatment and Prevention

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Objectives

• Understand how to integrate genetic and genomic information into oncology nursing practice

• Define the role of an oncology nurse in screening patients for hereditary cancer syndromes

• Understand the benefits and limitations of genetic and genomic testing

Genes

• Found in the DNA in each cell

• Controls
  – How cell functions
  – Grows
  – Divides
  – Lives

• Make proteins messengers for the cell
Cancer Is A Genetic Disease

Changes to genes that control the way our cells function

1. Acquired/Sporadic:
   - chemicals, radiation, viruses, age
   - damage genes during a person's life
   - cannot be passed to next generation

2. Inherited/Germline:
   - Passed directly from parent to child
   - mutation found in every cell of person's body

Genetic: Tumor Suppressor gene

- Limit cell growth
- Repair mismatched DNA
- Control when cells dies
- Mutated> cells grow uncontrollable
- Example: BRCA and p53

In hereditary cancer, one damaged gene is inherited.
DNA Repair Gene

- Fix mistakes made when DNA is copied
- Error> mistakes cannot be corrected>mutations>cancer
- Inherited: Lynch Syndrome
- Acquired/Somatic: oncogene

Oncogenes

- Normal State: directs cell growth
- Altered (mutated) State: promotes or allow uncontrolled growth
- Inherited or caused by environmental exposures to carcinogens
- Major molecular target for cancer treatment (HER-2, EGFR, BRAF)

Cancer Genomics

Genomic: identification of multiple genes, DNA sequences and proteins and their interaction with one another

AKA “Personalized Cancer Care”

Whole-genome sequencing of tumor to find somatic variants >explain cancer biology>targeted treatment
### Swedish Personalized Medicine 2014
- Integrate genomic information into patient care/research (emotional and physical supportive care)
- Molecular fingerprint of tumor
- Focused on set of gene alterations
- Tailored therapies/targeted clinical trials
- Adopted 2015 "Precision Medicine"

### Limitations
- Biological complexity: simple cause and effect are seldom found
- US Healthcare system (fee for service/barriers to change)
- Providers not well educated/prepared to provide in their practice
- Cost: Who will pay

### Limitations
- Patient data EMRs not well prepared
- Pharmaceutical companies transition (population based/precisely targeted)
- Rapid changes: How will this be approved/regulated
- Who needs to be part of the team to make these changes?

### Companion Diagnostics
"Provides information that is essential for the safe and effective use of a corresponding drug or biological product” [FDA website]
- Identify patient benefits
- Risk for serious side effects
- Monitor treatment
Companion Diagnostics

2014 the FDA issued “Guidance for Industry: In Vitro Companion Diagnostic Devices

- Identify the need for earlier stage in the drug development to plan for co-development
- The goal: stimulate early collaborations > result in faster access to promising new treatments

Companion Diagnostics

Medical tests paired with a specific drug

- BRCADx: BRCA (Olaparib) advanced ovarian
- HER2: FISH (Herceptin)
- BRAF: Melanoma (Vemurafenib)
- List of cleared and Approved on FDA website

Who is at High Risk for Hereditary Cancer?

Hereditary cancers account for a small but important proportion of all cancer

Why Test?

- NCCN guidelines recommend that all colon, uterine, ovarian, and uterine cancer patients be screened.
- Prevention of future cancers (targeted screening)
- Dominant mutation: only 50% of family will need increased screening.
“Red Flags” for Hereditary Breast and Ovarian Cancer

- Breast cancer before age 50
- Ovarian cancer at any age
- Male breast cancer at any age
- Multiple primary cancers
- Ashkenazi Jewish ancestry
- Relatives of a $BRCA$ mutation carrier
- Family History of Pancreatic cancer/Prostate Cancer
- Triple negative breast cancers

“Red Flags” for Hereditary Colorectal Syndromes

- History colon cancer diagnosed before age 60
- Endometrial cancer diagnosed before age 50
- Multiple family members with colon and other Lynch syndrome (endometrial, ovarian)
- FHx Colon cancer in a family member(s) diagnosed before age 50
- Polyposis in a relative(s) (>10 polyps in an individual in a lifetime)

Which Test To Order

- Single Gene: BRCA, Lynch
  $3000-4000$

- Cancer Panels: myRisk, Ambry, Color, ....
  $249-4000$

- Single Site
  $200-475$

Which lab to use? Myriad, Ambry, GeneDx, Invitae, Color, BROCA, etc.

Next Generations Cancer Panels

- Analyzes multiple selected genes

- Multiple rare genes that collectively account for a significant amount of hereditary cancer susceptibility.

- Helpful when family history shares features of several different hereditary cancer syndromes.

- High and Moderate Penetrance Genes
Spectrum of Mutations: Breast Cancer: ASCO Dec 2014

- 27,994
- 9.5% mutations
- 6.3% Lynch
- 2.1% genes not associated with breast

Study of Ovarian Cancer Patients

15.4% (100/648) patients with deleterious/suspected deleterious mutations

Four patients had two mutations

Presented at ASCO June 2014
Lucy R. Langer, MD, Heidi McCoy, MS, Kelsey Moyes, MStat, Jennifer Saam, PhD, Brian Abbott, MD, Larry J. Geier, MD

Advantages Panels

- Cost
- Do not need to rely on Pedigree to make decisions regarding testing
- Large amount of patients have limited knowledge regarding family history
- Result decreased months to 3 weeks
- Assess moderate and high penetrance genes
Limitations Genetic Testing

- Emotional
- Family Affair
- Limited knowledge about inherited condition
- Lack of guidelines
- Discrimination
- Unexpected results
- Cost

Variants

- Variant of undetermined significance:
  - Unable to tell if variant is harmful or harmless
  - Supreme court ruled that you cannot patent DNA
    Myriad does not need to share research on variants
  - “Free the Data”
  - Databases
  - Prompt Study

GINA Law

Protection for Medical Insurance
- Cannot drop patient or increase premiums

Does not cover
- Life insurance
- Disability Plans

All patients should be informed about Gina Law before testing

Insurance Coverage

- Coverage by Insurance
  - Medicare has criteria for BRCA, Lynch, and AFAP and is covered 100%

- Affordable Care Act: Required to cover genetic testing

- Insurances all have policies/medical criteria
Cost Cancer Treatment

Komen

$22,000 early stages
$120,000 stage 3-4 per
$98,571 per year metastatic breast cancer

NCI (2010) Initial/Cancer Death

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Cost Initial ($)</th>
<th>Cost Cancer Death ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon cancer</td>
<td>$51,812</td>
<td>$85,671</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>$82,324</td>
<td>$99,715</td>
</tr>
<tr>
<td>Uterine cancer</td>
<td>$26,775</td>
<td>$70,175</td>
</tr>
</tbody>
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Let Me Tell You A Story

To Test or Not To Test

- Increase surveillance
- Chemoprevention
- Prophylactic Surgery

Risk Reducing Oophorectomy

- ~96% ovarian cancer risk reduction in BRCA carriers
- Can reduce breast cancer risk by up to 68%
- Recommend bilateral salpingo-oophorectomy (BSO) after childbearing is completed or at age 35-40
- Salpingectomy only not standard of care (clinical trials)
**Screening for Lynch Syndrome:**

*MSI and IHC*

- MSI and IHC testing can be used as screening tools and are not diagnostic for Lynch syndrome.
- Some centers are testing all selected or completing universal testing. Check your institution's policy.

<table>
<thead>
<tr>
<th>Sporadic cancer*</th>
<th>Lynch syndrome-related cancer*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal &amp;</td>
<td>10-15%</td>
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<tr>
<td></td>
<td>Up to 90-95%</td>
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**Lynch Syndrome Increases Risks of Other Cancers**

- Endometrial (25-60%)
- Ovarian cancer (4-24%)
- Gastric cancer (1-13%)
- Additional cancers with a lifetime risk of <5%
  - Ureter/renal pelvis
  - Biliary tract
  - Small bowel
  - Pancreas
  - Brain
  - Sebaceous adenoma
- MSH6 and PMS2 different recommendations

**Rationale for Frequent Colonoscopy**

- Accelerated progression from adenoma to cancer
  - HNPCC, 1-3 years
  - General population, 5-10 years
- Reduces CRC risk by more than 50%, overall mortality reduced by 65%

**It’s Just Not About Colon Cancer**
Role of Oncology Nurse: Position Statement ONS

- Interpret test results
- Understand the benefits and limitations
- Keep updated on new testing available
- Educate patients clinical utility and accurate interpretation (treatment/recommendations)
- Advocate for Informed Consent (pre and post counseling)
- Know your local referrals/resources for genetics

Consumer Genetic Testing

Scientific American 2013: 23andMe Is Terrifying, but Not for the Reasons the FDA Thinks
The genetic-testing company’s real goal is to hoard your personal data

Goal: genetic blueprint, insight into ancestry, genealogy and inherited traits
Edging closer to marketing they could predict or prevent health problems
FDA approval for “medical device”
Compares to Google: data storage > advertiser target you
Are they the “Google” of our personalized health information
Companies goal: medical research

23andME

- FDA approved 2015
- Identifies Single nucleotide polymorphisms (SNPs)
- Typographical errors
- 10 million SNPs in genetic code
- Impact on traits, response to drugs, risk for disease
- Found traits (odds of eye color, taste bitterness, ancestral heritage)
- Until Nov 2013 (obesity, macular degeneration, alcoholism, breast cancer)

23andMe

Reports offered guidance to reduce health risk
Concerns: interpretations accurate, make bad medical decisions
23andME today:
Offers 36 tests approved by FDA versus 254
Price is now $199 versus $99
Connect with DNA relatives
Focus on “carrier status” reports (sickle cell, cystic fibrosis)
Prohibit to tell if you will develop disease
Future: develop new drugs, allergies to medications, risk for diseases
Resources

- Genomics: Dr. Anna Berry director of Molecular Pathology at CellNetix.
- NCCN guidelines: Genetic/Familial High-Risk Assessment: Breast and Ovarian, and Coloorectal
- ONS: Cancer Genetics Course 16.3 contact hours $199
- genetests.org
- www.genome.gov