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

Chromosomes are single pieces of DNA that contain many genes. DNA is a molecule that carries genetic information. Genes contain instructions for how to make proteins. Proteins act alone or in groups to perform many functions.
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
**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

- BRCACDx: 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
HCP Genes by Cancer Type/Associated Syndrome

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<thead>
<tr>
<th>Syndrome Name</th>
<th>Breast Cancer</th>
<th>Ovarian Cancer</th>
<th>Colon Cancer</th>
<th>Endometrial Cancer</th>
<th>Melanoma</th>
<th>Pancreas Cancer</th>
<th>Gastric Cancer</th>
<th>Prostate Cancer</th>
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<td>MUTYH-associated Colon Cancer Risk; MUTYH-associated Polyposis Syndrome (MAP)</td>
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Study of Ovarian Cancer Patients

15.4% (100/648) patients with deleterious/suspected deleterious mutations. Four patients had two mutations.

Spectrum of Mutations: Breast Cancer: ASCO Dec 2014

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

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
- Long term

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 Per Year</th>
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<tbody>
<tr>
<td>Colon cancer</td>
<td>$51,812/$85,671</td>
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<tr>
<td>Ovarian cancer</td>
<td>$82,324/$99,715</td>
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<tr>
<td>Uterine cancer</td>
<td>$26,775/$70,175</td>
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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.

<table>
<thead>
<tr>
<th>Sporadic cancer*</th>
<th>Lynch syndrome-related cancer*</th>
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<tbody>
<tr>
<td>10-15%</td>
<td>Up to 90-95%</td>
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- Some centers are testing all selected or completing universal testing. Check your institutions policy.

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%
  - Uter/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”
Compared 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