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All in the Family: Genetics of Prostate Cancer


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Genetics “Lingo”

- Gene
- Chromosome
- DNA
- Genetic
- Hereditary
- Sporadic
- Mutation



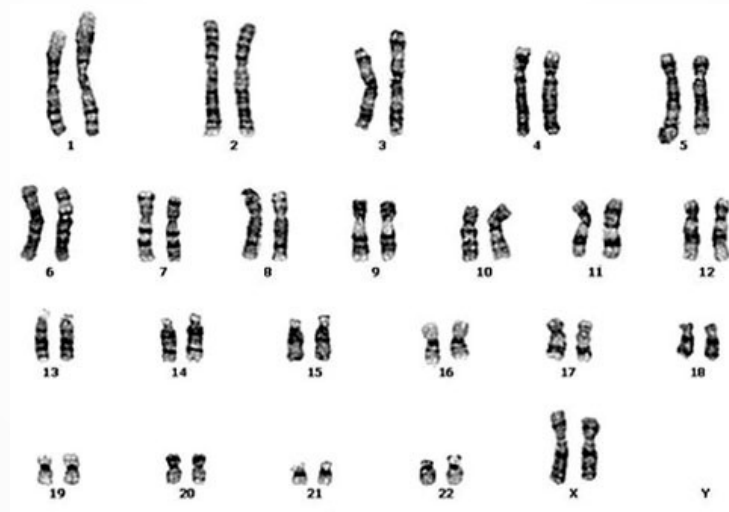
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~ 25,000 Genes in every cell

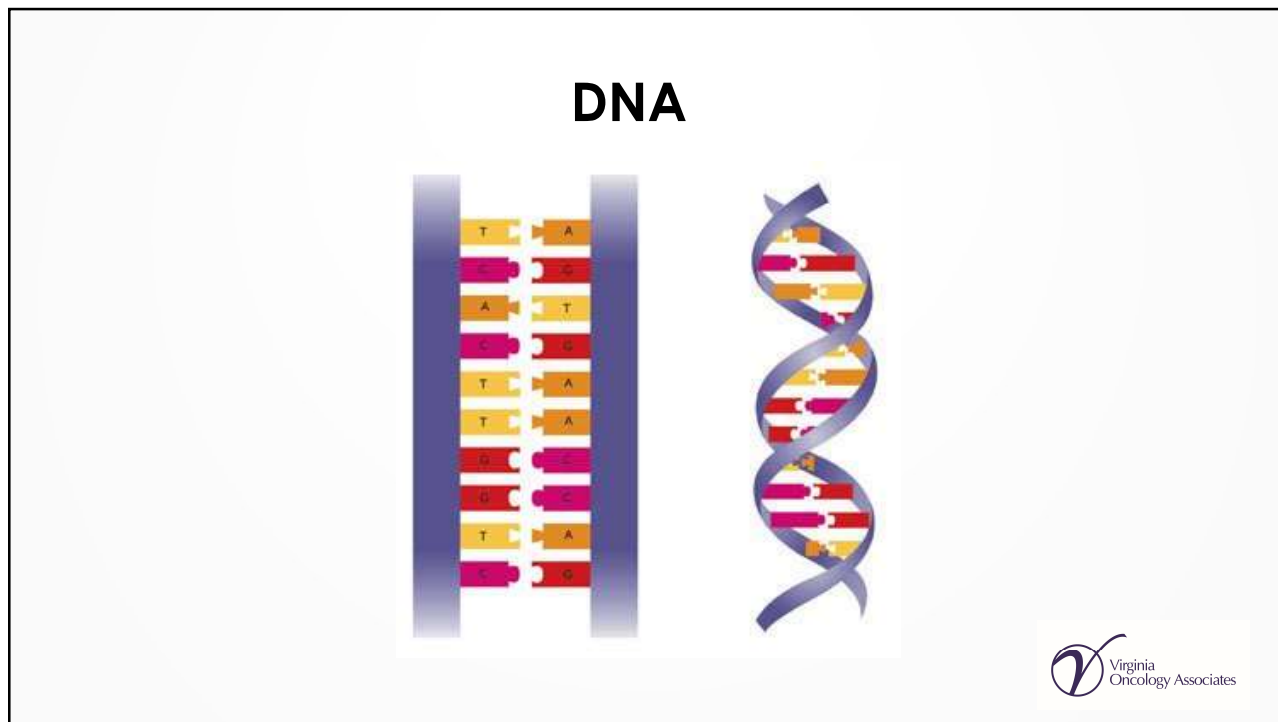


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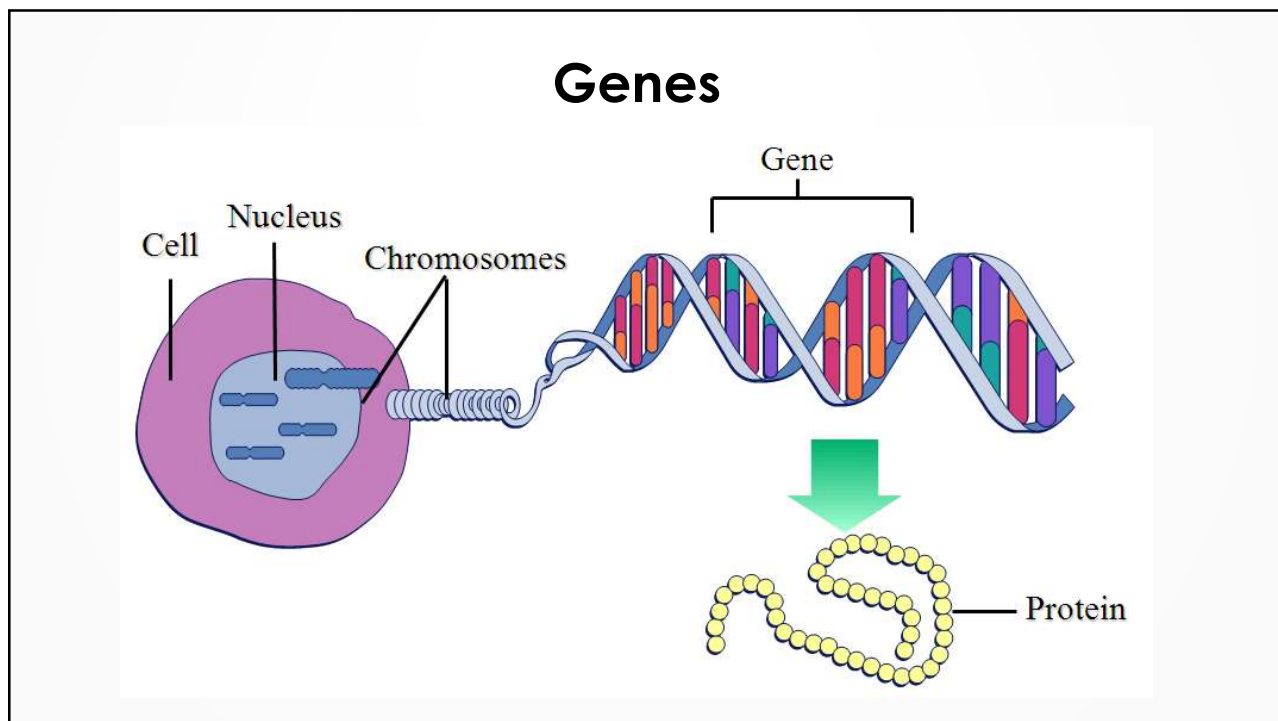
Chromosomes



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Cancer is a Genetic Disease

- ALL cancer is genetic.
- Mutations in genes lead to cancer development.
- These mutations can be acquired or inherited.
- Testing for these gene mutations can guide therapy and/or cancer screening.

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Mutation-Permanent change in your DNA

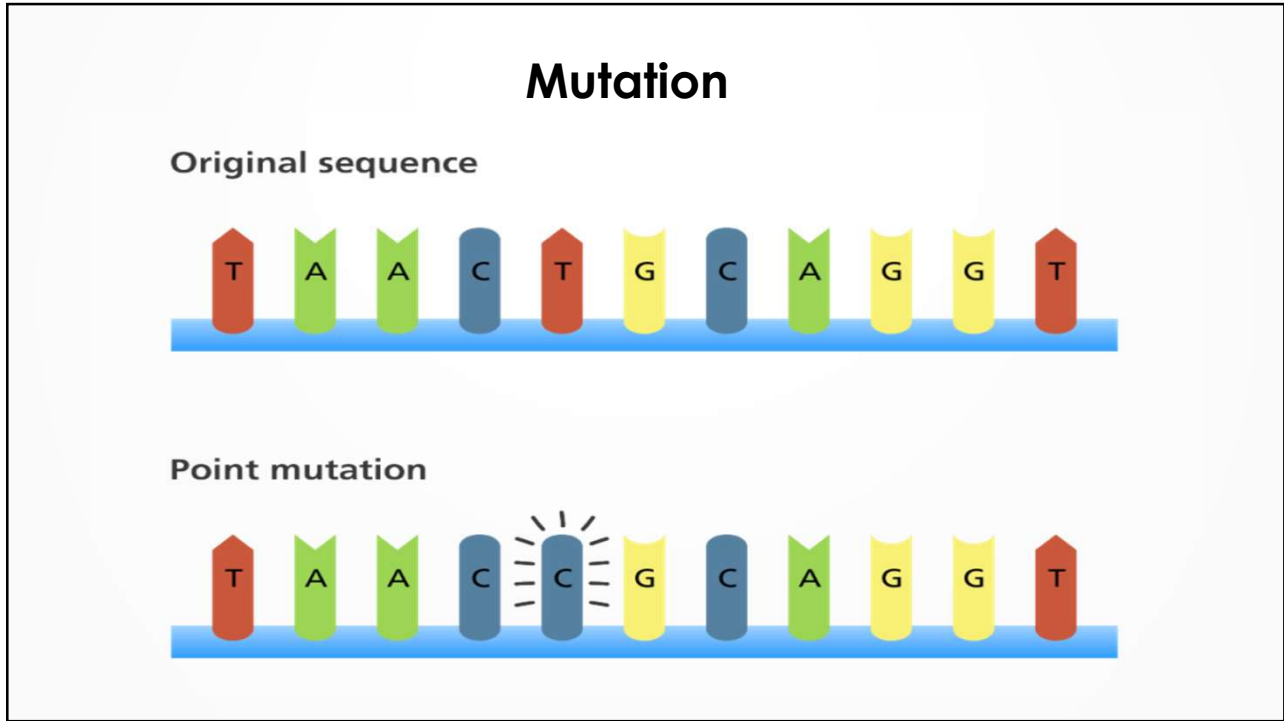
Sporadic

- Occur over time
- Usually confined to a specific organ
- Not passed on to offspring

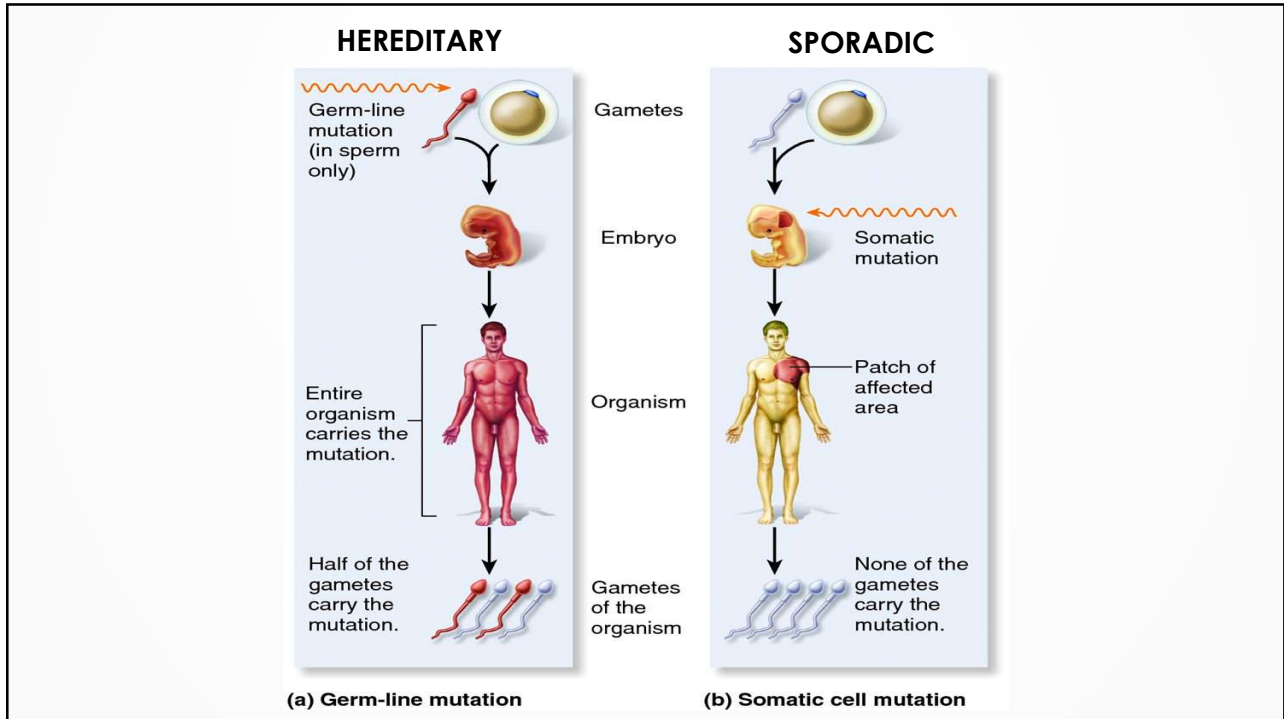
Hereditary

- Inherited from mother or father
- Found in every cell of the body
- Can be passed on to offspring

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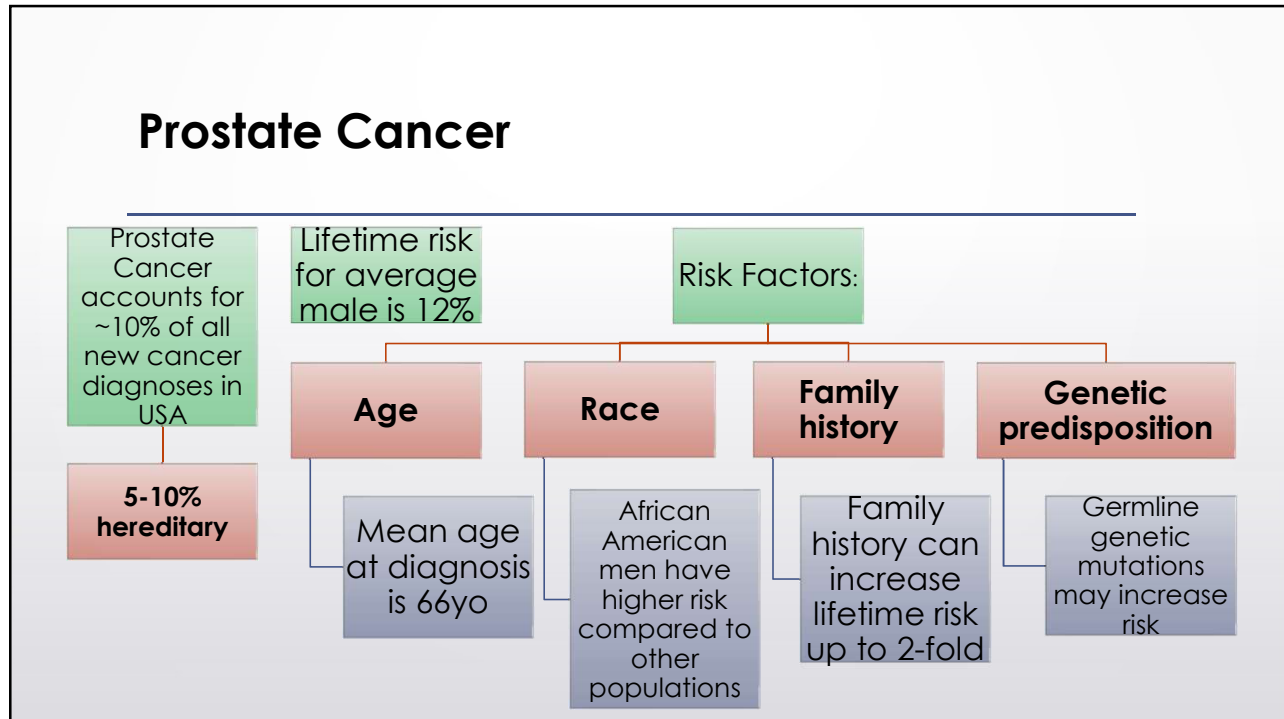


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Prostate Cancer



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Is Prostate Cancer Genetic?

- Yes, prostate cancer is genetic!
- Although, it is not always hereditary.
- In general, ~5-10% of cancers are hereditary.
- In one study an inherited gene mutation was identified in 17% of men tested with prostate cancer (unselected population).
- Another study found that 8.8% to 18.5% of patients with metastatic disease had an inherited gene mutation.

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Red-Flags For Hereditary Cancer



- Early age at onset (≤ 50)
- Multiple primaries in same individual
- Vertical transmission (multiple generation affected)
- Gleason score ≥ 7 and/or metastatic disease
 - ~8-12% of men with metastatic prostate cancer may carry a germline mutation
- Multiple other primary cancers in same family (paternal or maternal)



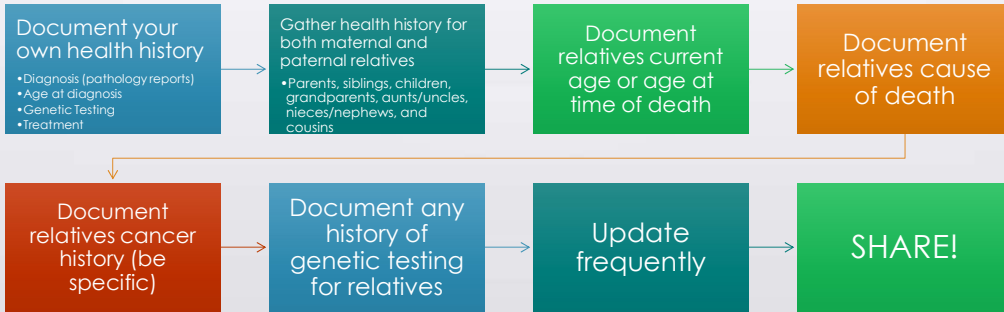
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The Family History

- Family history is one of the most important screening tools we have for cancer.
- Having a family history of cancer can increase a person's overall lifetime risk substantially above general population risk.
- Knowing and sharing your family history can be lifesaving!

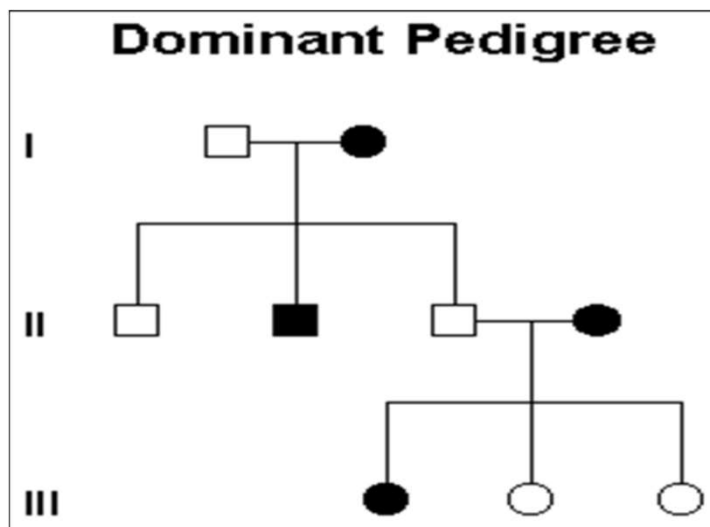
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How to Take a Family History

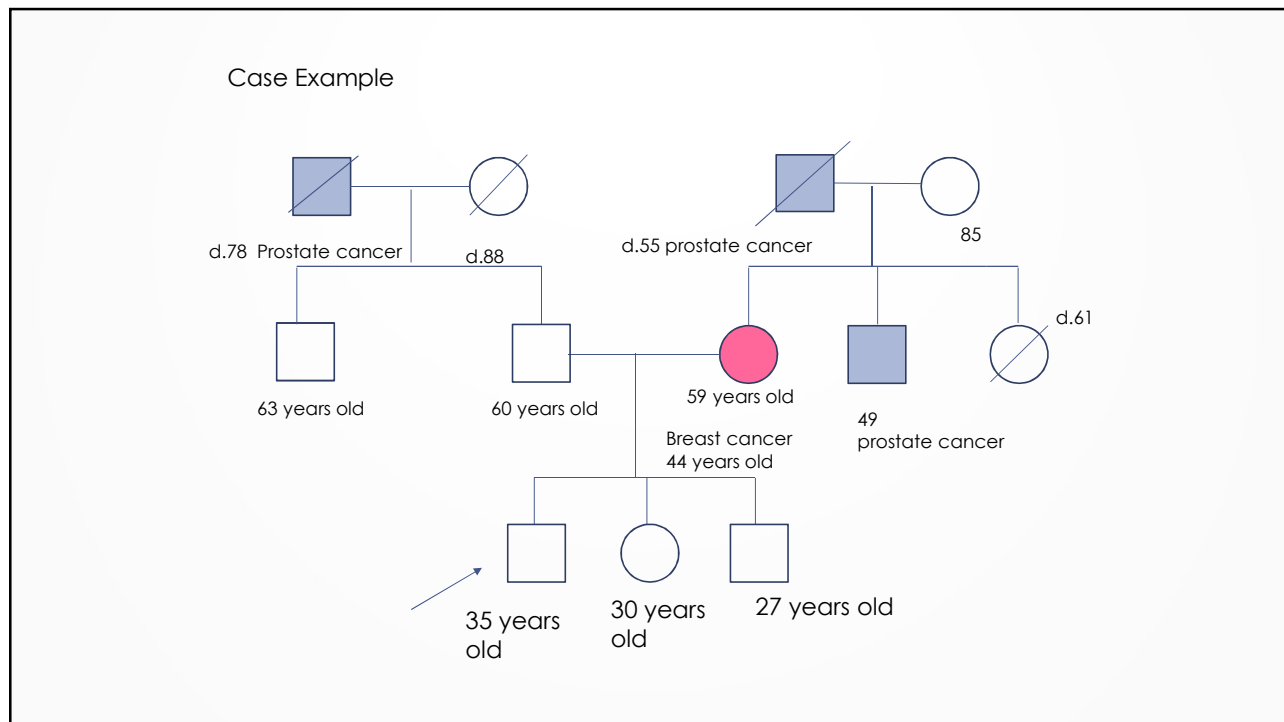


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Autosomal Dominant



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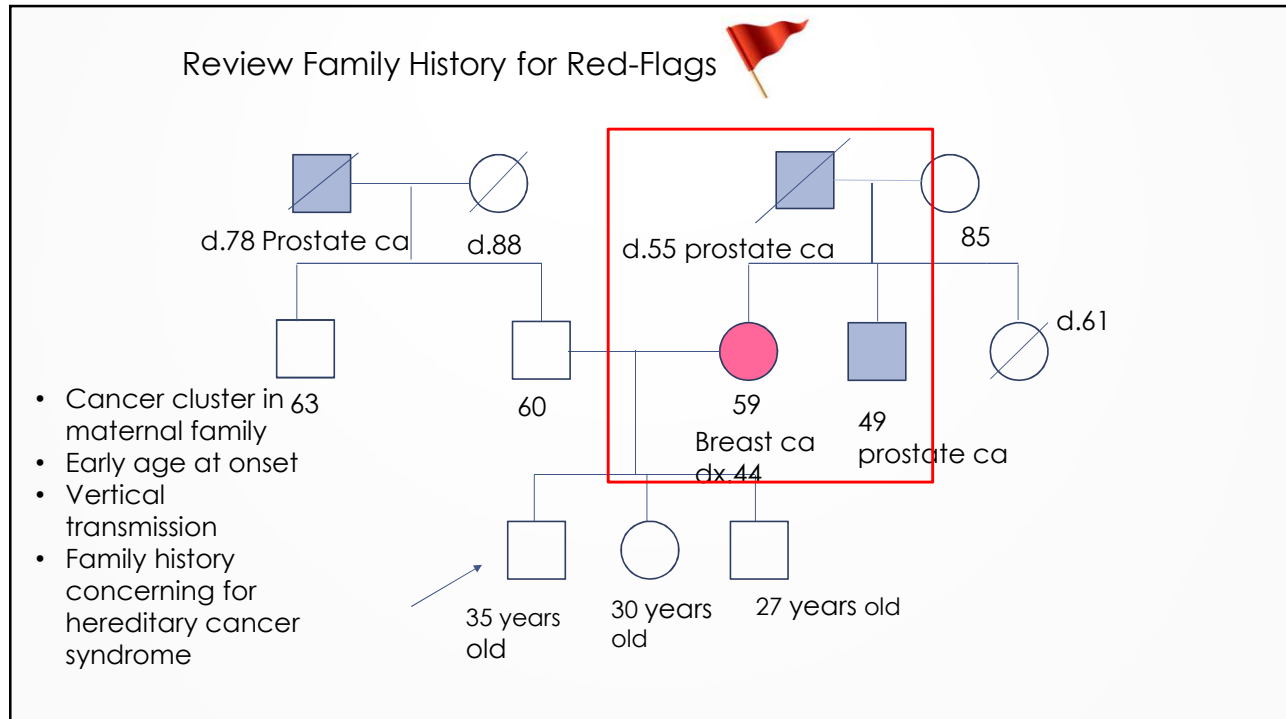
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Genetic Counseling Workup

- Patient is a 35 y.o. healthy white male
- Family history is positive for breast and prostate cancer
- No genetic testing in family
- Patient has not started cancer screening
- Patient wants to know if he should have genetic testing

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Genetic Syndromes Associated with Prostate Cancer

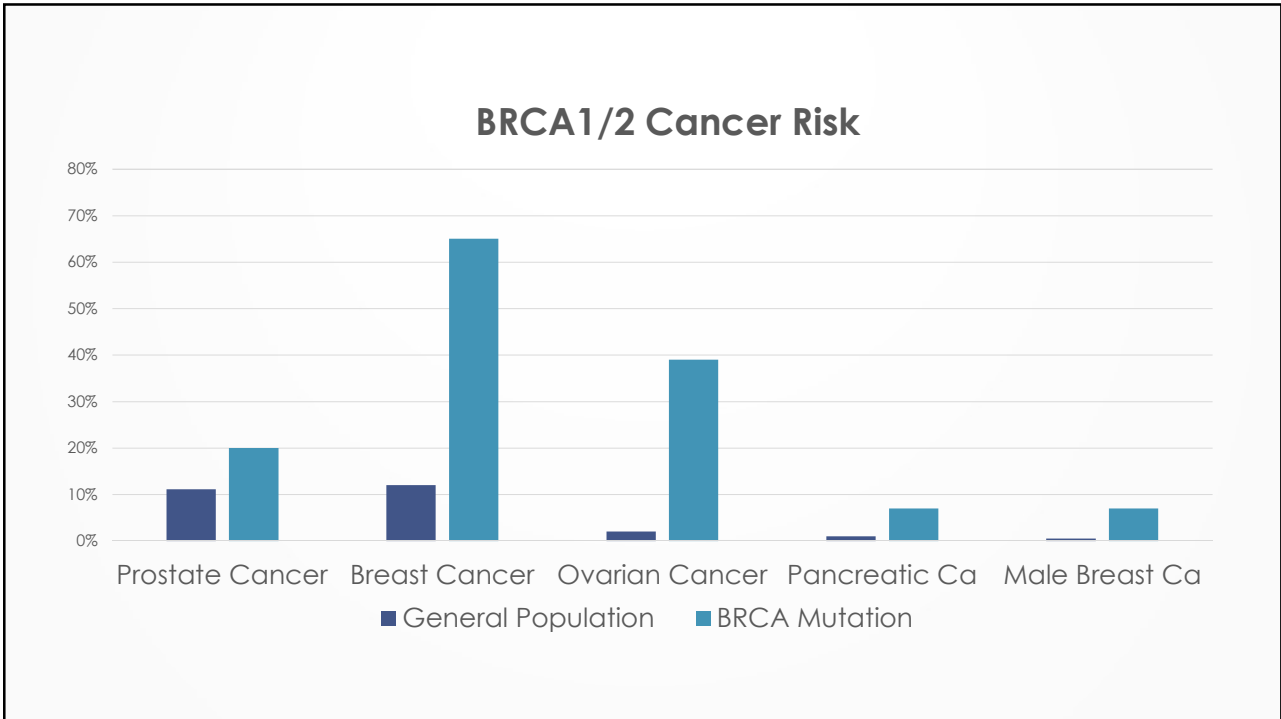
- BRCA1/2
 - BRCA2 associated with clinically aggressive prostate cancer
 - Potential targeted therapeutic options
- HOXB13
 - One specific variant (G84E)
- Mismatch Repair genes
 - Lynch syndrome (colon cancer risk)
- Other genes
 - ATM, CHEK2, NBN

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Hereditary Breast and Ovarian Cancer syndrome

- BRCA1 and BRCA2
- Breast cancer (male and female), ovarian cancer, prostate, melanoma, and pancreatic cancer
- Autosomal dominant inheritance
- 1 in 40 incidence in Ashkenazi Jewish population
- ~1 in 500 incidence in general population

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BRCA Positive Medical Management (Males)

- Breast self-exam training and education starting at age 35
- Clinical breast exam, every 12 months, starting at age 35
- Prostate Cancer screening starting at age 45
- Germline mutations in BRCA1/BRCA2 may guide therapy decisions in metastatic cases (PARP inhibitors)

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BRCA Positive Medical Management (Females)

- Breast self-exam training and education starting at age 18
- Clinical breast exam, every 6-12 months, starting at age 25
- Breast Screening
 - Annual breast MRI (25-29 years old)
 - Annual mammogram (30-75 years old)
- Option of risk-reducing mastectomy
- Risk-reducing salpingo-oophorectomy

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Patient is Tested...now what?



Patient has positive test result Gene mutation identified



Recommend changes to his cancer screening

Screen early and more frequently
Target screening to specific organ(s) based on results

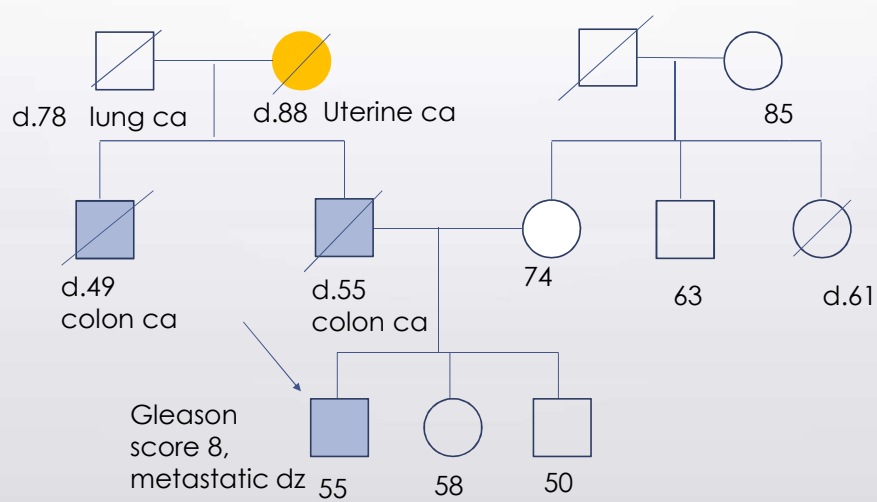


Recommend genetic testing for his family members

1st degree relative have 50% risk to have gene mutation
Applies to males and females

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Case Example #2



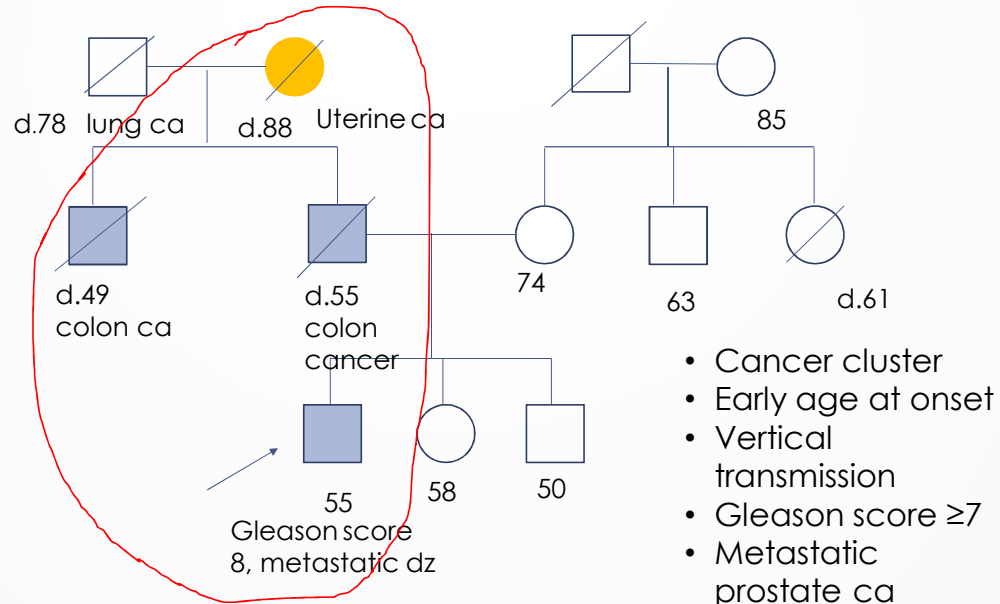
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Genetic Counseling Workup

- Patient is a 55 y.o. AA male with a diagnosis of metastatic prostate cancer.
- Family history is positive for colon and uterine cancer.
- No genetic testing in family.
- Patient wants to know if he should have genetic testing.

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Review Family History for Red-Flags



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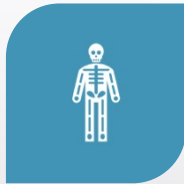
Genetic Syndromes Associated with Prostate Cancer

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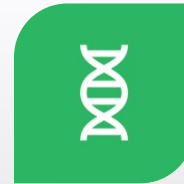
Lynch syndrome



MLH1, MSH2,
MSH6, PMS2, AND
EPCAM

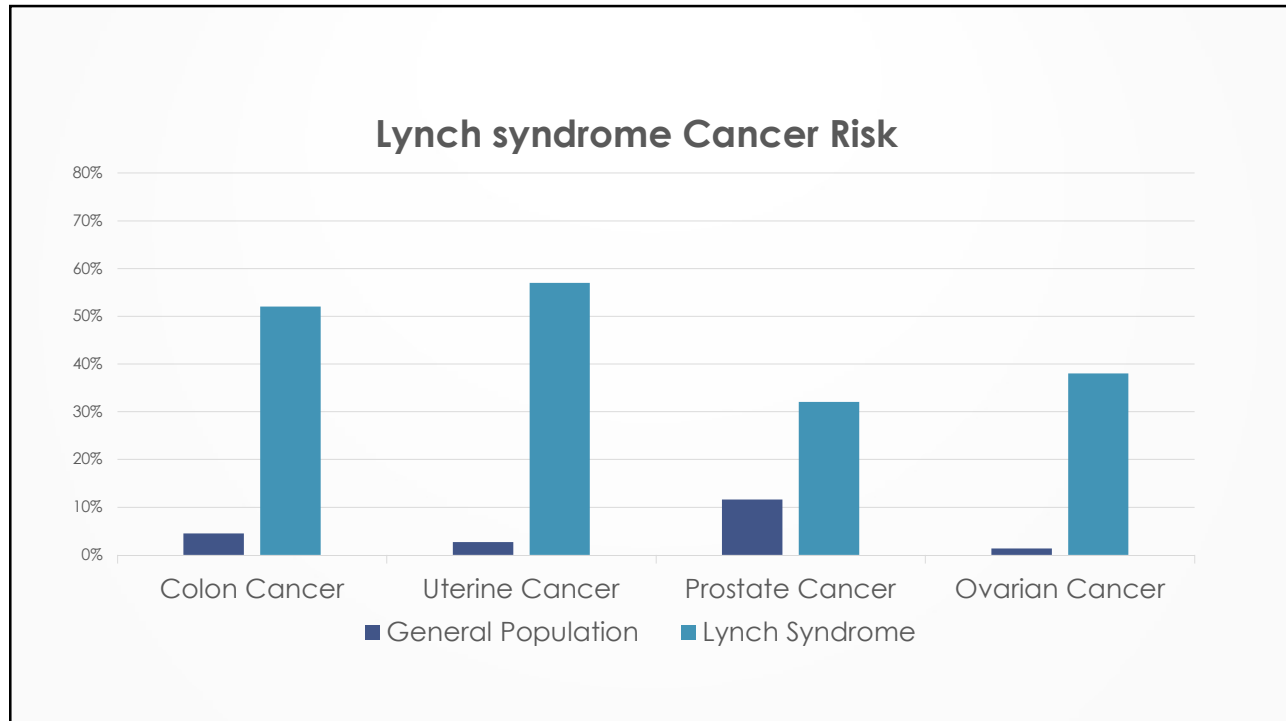


COLON, UTERINE,
OVARIAN, STOMACH,
PROSTATE,
PANCREATIC, AND
OTHERS



AUTOSOMAL
DOMINANT
INHERITANCE

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Lynch Syndrome Management

- Colonoscopy at age 20-25 years old every 1-2 years
- Hysterectomy and Bilateral salpingo-oophorectomy may be considered
- **Insufficient evidence to recommend earlier or more frequent prostate screening; however, men with Lynch syndrome should be encouraged to participate in prostate screening**
- No specific screening recommendations for pancreatic cancer

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WHY?



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Precision Medicine

- Precision Medicine-"an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person."
 - Genetic
 - Somatic
 - germline
 - Environmental
 - Behavioral

Precision Medicine Initiative

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The Why...

Patient

- Testing can guide therapy
- Learn risk for other cancers
- Adjust future cancer screening
- Inform relatives


Family

- Proactive early screening
- Modify lifestyle behaviors
- Consider risk-reducing surgical options
- Avoid unnecessary screening

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When To Consider Genetic Testing

 Personal history of metastatic prostate cancer

 Personal history of high-grade prostate cancer (Gleason score ≥ 7) at any age with family hx of prostate, breast, ovarian, or pancreatic cancer

 Ashkenazi Jewish ancestry and personal or family hx of prostate ca

 ****It's always best to start testing with an affected individual before testing unaffected relatives.****

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What Does Genetic Counseling/ Genetic Testing Involve?



**Consult with
healthcare
professional
trained in medical
genetics**



**Blood draw or
saliva sample**



**Results available in
2-3 weeks**

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Insurance Coverage/Discrimination

- Most insurance companies provide coverage for genetic testing when medical necessity is established and testing will guide medical management.
- Cost for genetic testing has drastically decreased in cost over years.
- Most laboratories offer discounted testing for relatives once gene mutation is identified.
- GINA (Genetic Information Nondiscrimination Act 2008) protects against genetic discrimination.
 - Does not apply to life, disability, or long-term care insurance.
 - Does not apply to active duty military.



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Additional Resources

- www.cancer.net
- www.facingourrisk.org
- www.cancer.org
- <http://www.hhs.gov/familyhistory>
- http://www.marchofdimes.com/pnhec/4439_1109.asp



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Questions?



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