Cancer Biology, Pathology and Genetic Predisposition

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Disclosure

- I have no conflicts of interest in relation to this program or presentation.

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Objectives

- Define cancer and associated terminology
- Review how cancer occurs and summarize cancer risk factors
- Recognize red flags of hereditary cancer syndromes and which patients should consider hereditary cancer genetic testing

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History of Cancer

- Imhotep (2625 BCE)
  - Egyptian physician
  - “bulging mass in the breast”
  - Therapy: “there is none”
- Atossa (440 BCE)
  - Queen of Persia
  - Bleeding lump in breast
  - Greek slave removed the tumor
- Chiribaya tribe (700 CE)
  - Atacama desert in Peru
  - “Bulbous mass” in upper left arm

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Cancer Background

- Definition
  - "Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body"- National Cancer Institute
- Two main categories
  - Hematologic cancer
  - Solid tumor cancer
- Not a single condition, but actually 100s of different diseases

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Cancer Incidence

- According to the American Cancer Society, the estimated number of new cancer cases in 2022 will be 1,918,030 in the US and 35,130 in MN
  - #1 most common- breast cancer
  - #2 most common- prostate cancer
  - #3 most common- lung cancer
- Lifetime risk of cancer: ~40% for males and ~38% for females (based on 2016-2018 data)
- Median age of diagnosis: age 66

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Cancer Terminology

- Tumor: a mass of tissue that results from abnormal cell growth and division
  - Benign- not cancerous, cells don't spread to other areas of the body
  - Malignant- cancerous, cells will invade or spread to other areas of the body
- Carcinoma: cancer that begins in the skin or tissues that line internal organs
- Sarcoma: cancer that begins in the bone or connective tissue
- In situ: "in the original place", no penetration of the basement membrane

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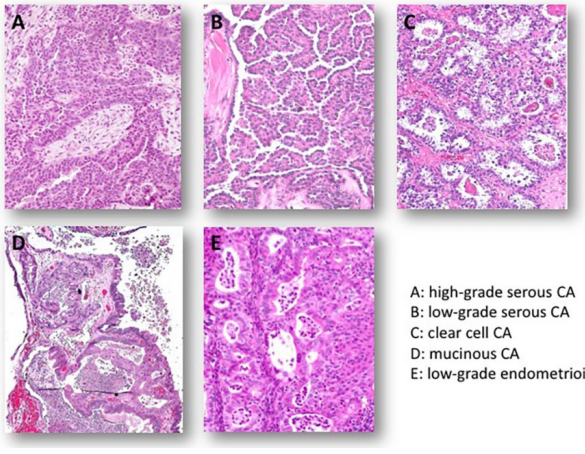
Cancer Pathology



A: high-grade serous CA
B: low-grade serous CA
C: clear cell CA
D: mucinous CA
E: low-grade endometrioid CA

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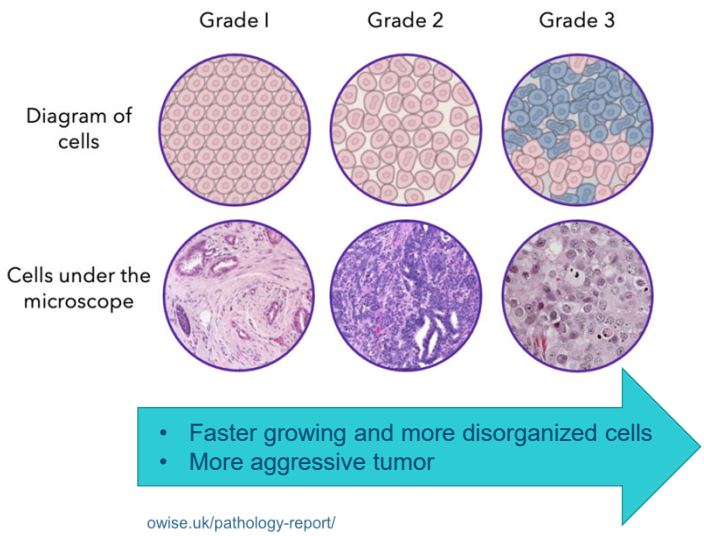
Cancer Grade



owise.uk/pathology-report/

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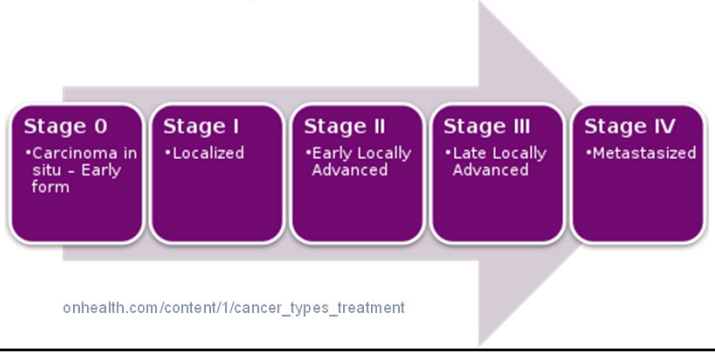
Cancer Stage

- Stage 0 to IV
  - Stage 0: abnormal cells that haven't spread (aka in situ)
  - Stage I-III: cancer that hasn't spread beyond the site of the primary tumor or have only spread to nearby tissue
  - Stage IV: cancer has spread to distant areas of the body



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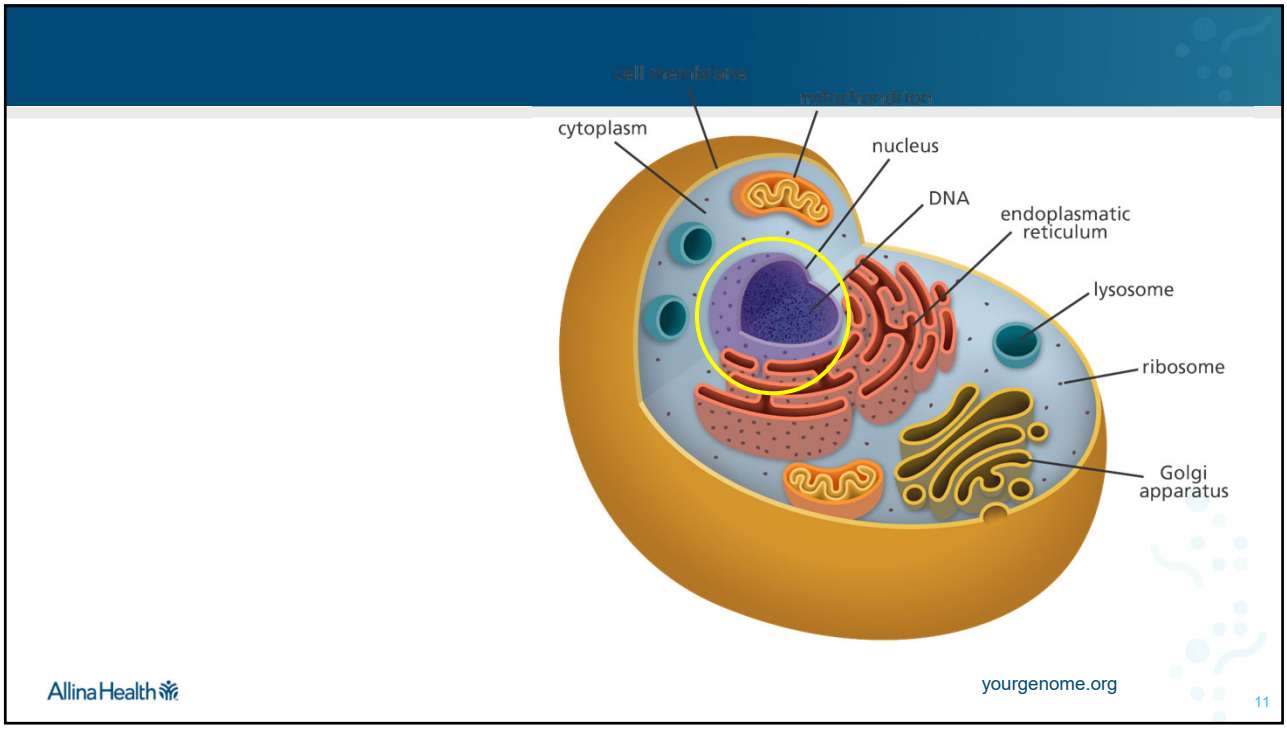
cell membrane
mitochondrion
cytoplasm
nucleus
DNA
endoplasmatic reticulum
lysosome
ribosome
Golgi apparatus
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yourgenome.org
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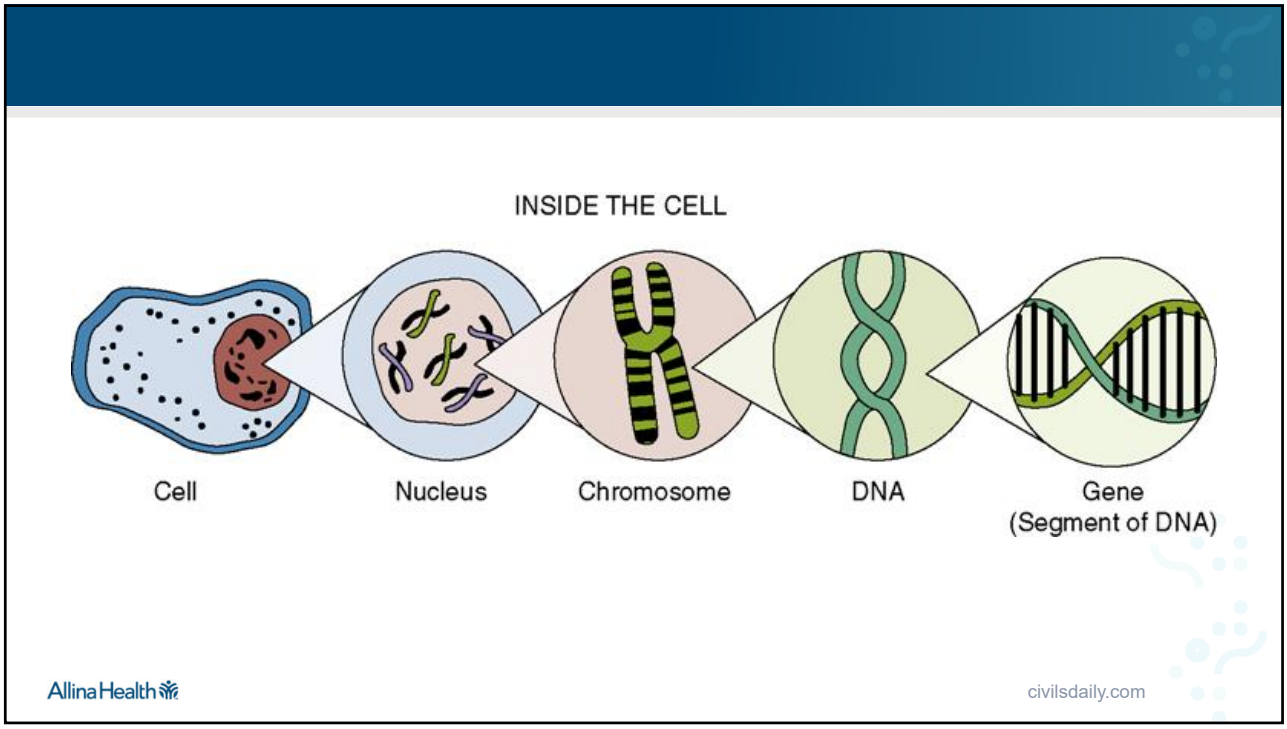
INSIDE THE CELL
Cell
Nucleus
Chromosome
DNA
Gene
(Segment of DNA)
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civilsdaily.com

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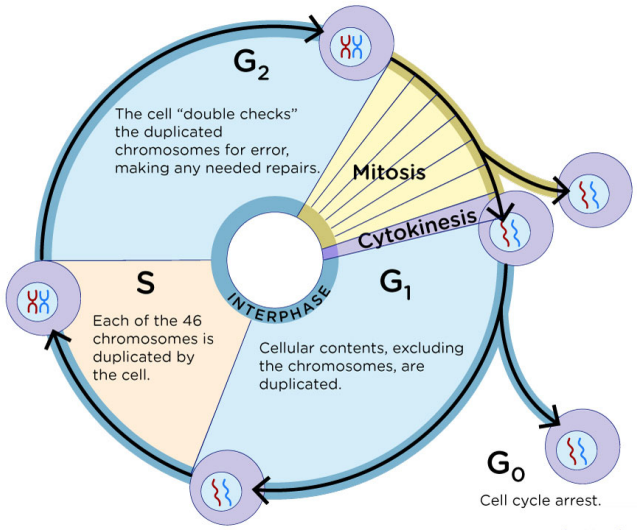

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Cell Cycle Regulation

- DNA repair genes
  - Fix errors made during DNA replication
  - Inactivation leads to cancer development
  - Ex: *MLH1, MSH2, MSH6, PMS2*
- Tumor suppressor genes
  - Negatively regulate the growth of cells
  - Inactivation leads to cancer development
  - Ex: *BRCA1/2*
- Oncogenes
  - Play roles in cell cycle regulation
  - Activation leads to cancer development
  - Ex: *RET*

labs.wsu.edu

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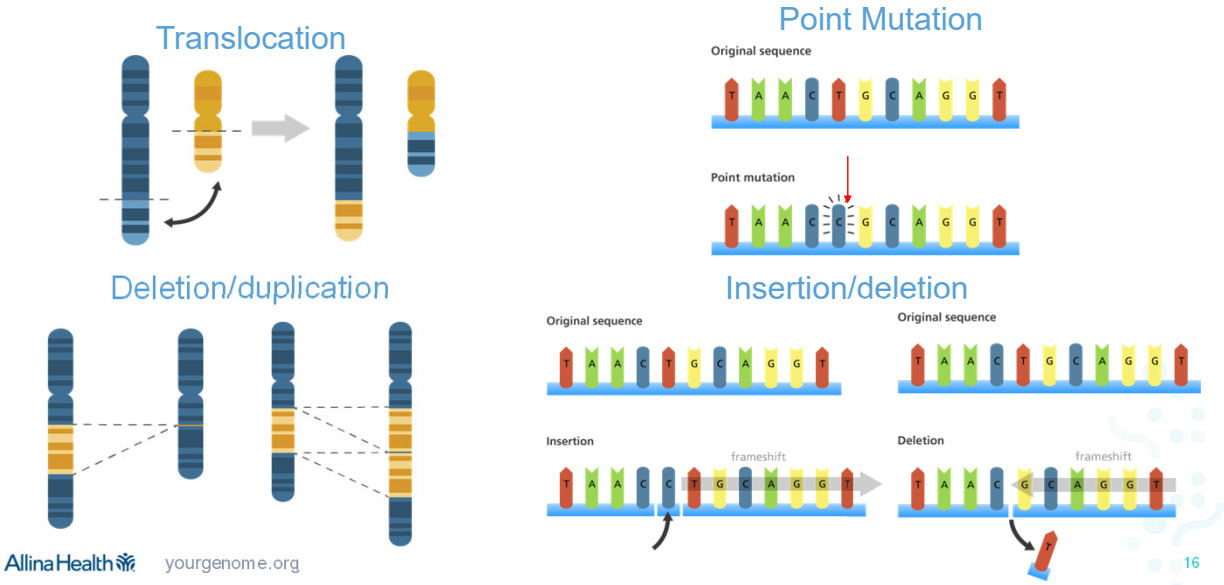
Types of Gene Mutations



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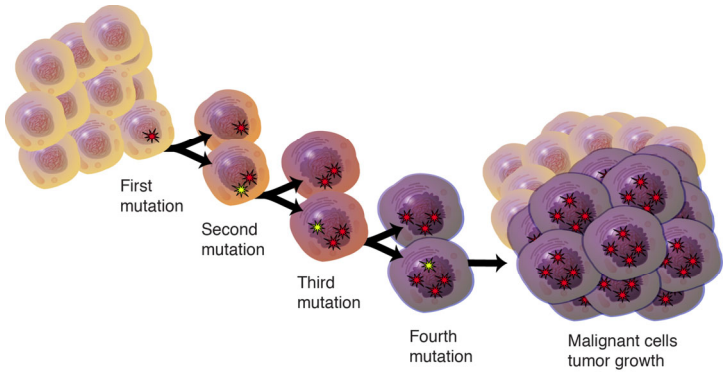
Cancer: A Genetic Disease



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dnascience.plos.org

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Cancer Risk Factors

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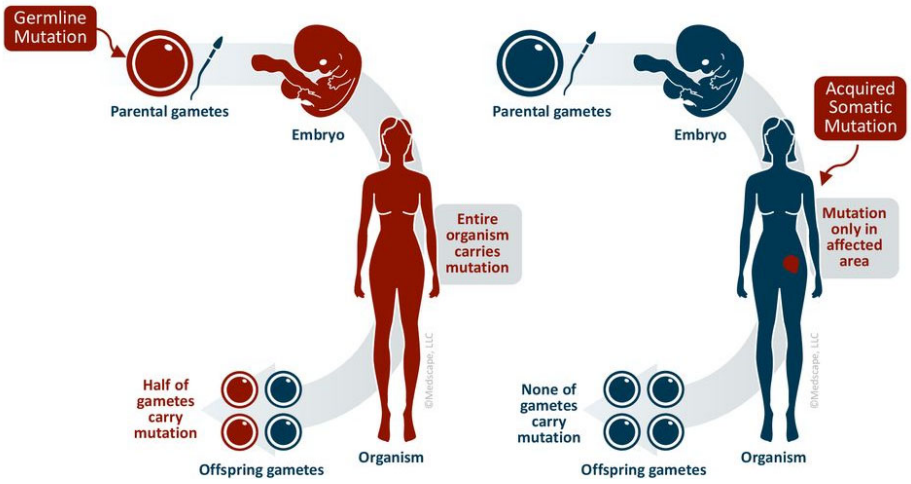
Cancer: Genetic, But Not Always Inherited



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Medscape

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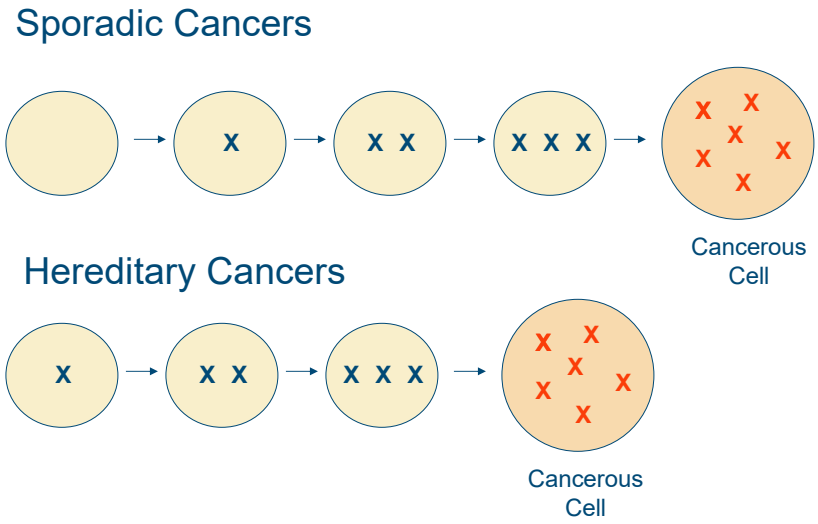
Cancer: Genetic, But Not Always Inherited



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Cancer: Genetic, But Not Always Inherited

Germline mutations	Somatic mutations
• Occur initially in the egg or sperm	• Occur in non-germline cells (ex: breast, colon, lung, etc.)
• Are inherited	• Not inherited
• Mutation is present in all cells of the body	• Mutation is only present in some cells in the body
• ~5-10% of all cancers are hereditary	• ~90-95% of all cancers are sporadic

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