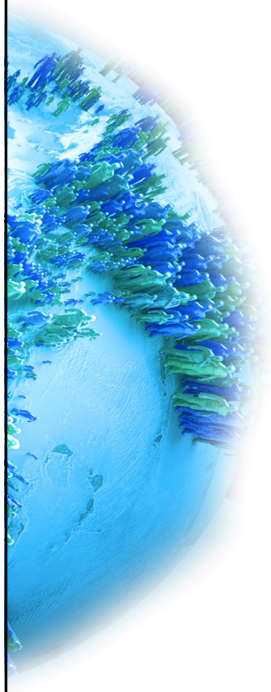
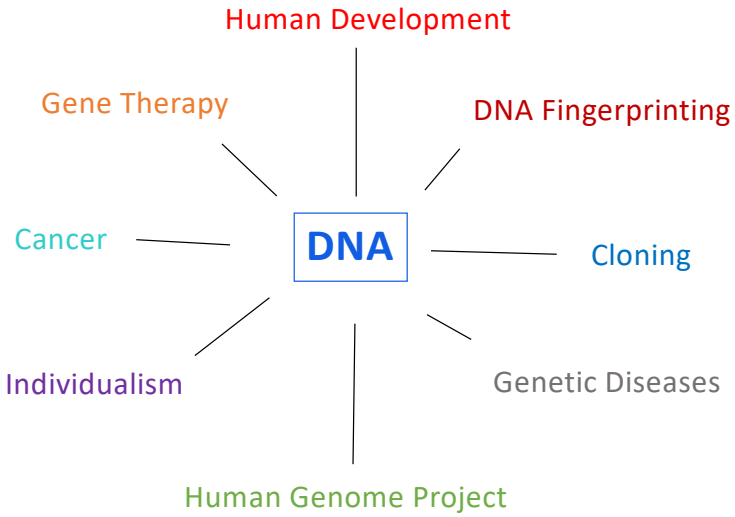


Breast Cancer and DNA

Today's Lecture

1

DNA is central to all aspects of Biology



- To understand modern Biology, you need to understand DNA.

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DNA is the "Blueprint for Life"

Each person has a unique complement of **DNA**

↓ which causes

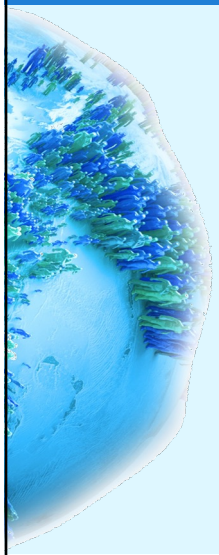
Each person to have a unique complement of **proteins**

↓ which contributes to

Each person having a **unique appearance and behavior**

3

Overview of Lecture



- Humans as hunks of protein
- DNA and protein synthesis
- Mitosis and Cancer
- Breast Cancer

4

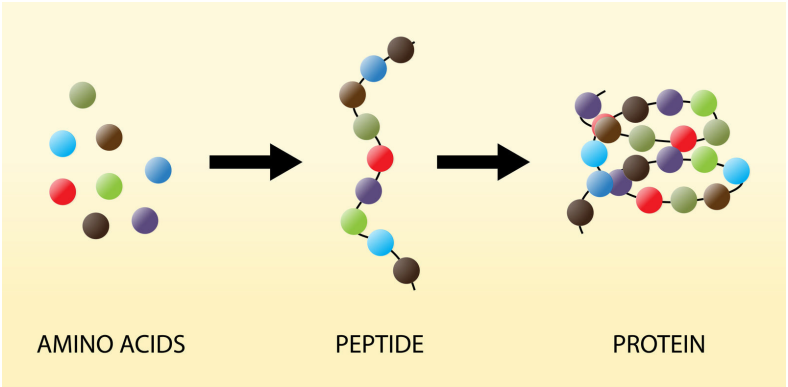
Functions of Protein

Humans are made of about 2 million different types of proteins

- **Structural**
  - muscle, hair, connective tissue, bone
- **Chemical**
  - antibodies, hormones, enzymes
  - Chemical reactions in cells are regulated by enzymes

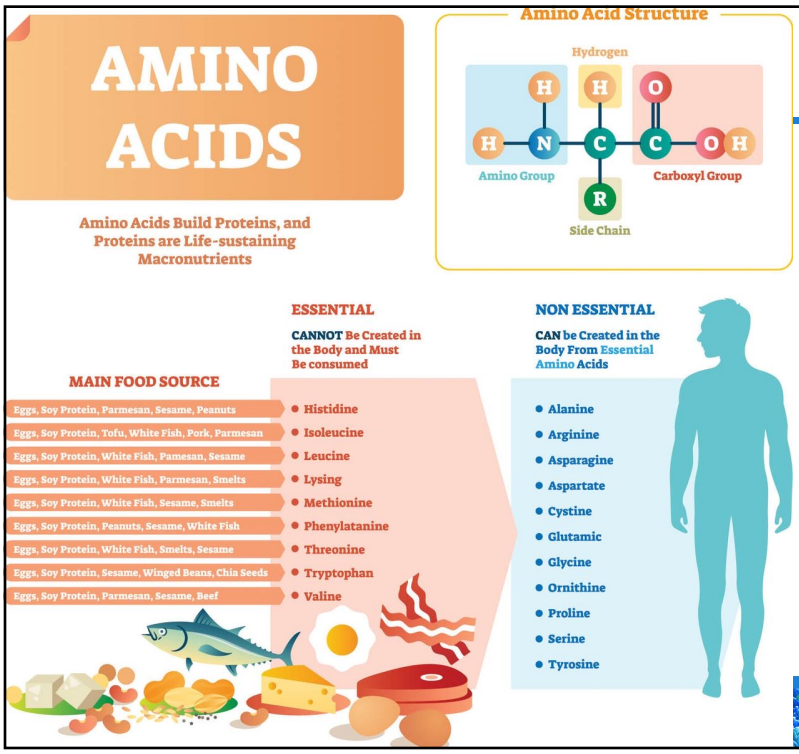
5

What are proteins made of?



- Proteins are chains of amino acids
- Amino acids join to form peptides (short proteins)
- Proteins range from a few hundred amino acids to thousands of amino acids

6

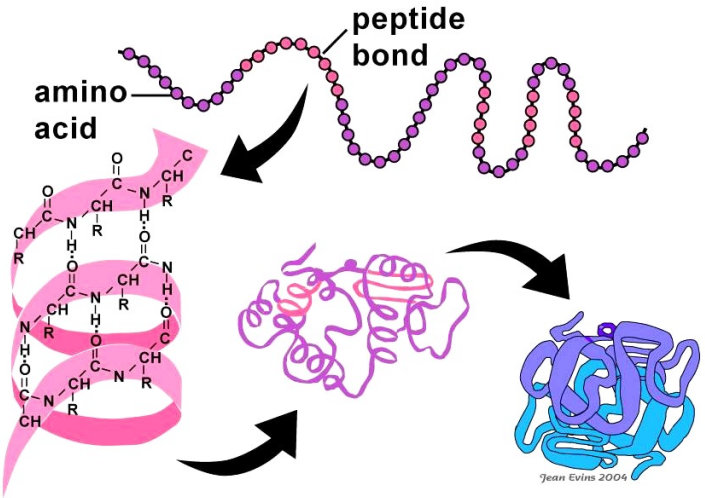


Amino Acids

- There are **20 different Amino Acids** found in humans
- About half of the amino acids are considered "**essential**," meaning you must consume them in food
- The other half can be synthesized by your body

7

Protein Structure



- Proteins are much more than just strings of amino acids.
- For a protein to function normally, it must be shaped exactly right.
- This requires that the "chain" of amino acids be folded up into the precise 3-dimensional shape.

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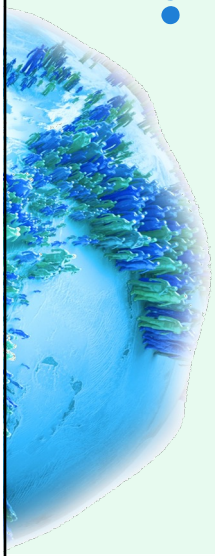


How does the human body make two million different proteins with only 20 different amino acids?

Answer...

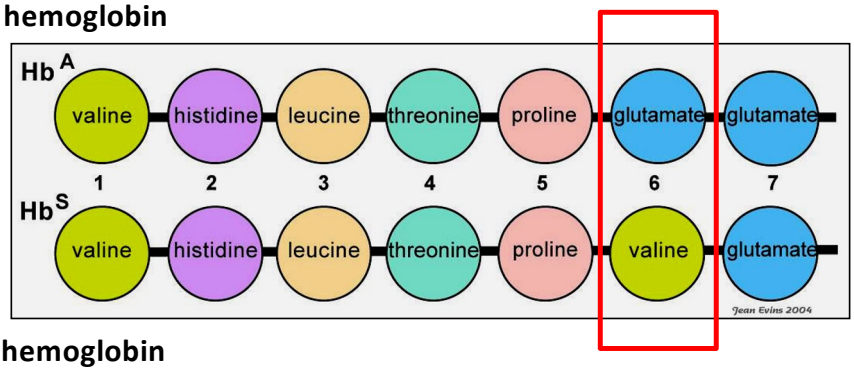
By varying the sequence of amino acids in a protein.

The function of each protein is determined by its structure (amino acid sequence and folding)

9

Amino Acid Sequence of Hemoglobin

Normal hemoglobin



Sickle-cell hemoglobin

Box above shows the one amino acid difference in normal hemoglobin versus sickle-cell hemoglobin

10

Proteins are made by stringing together _____.

A. Nucleotides
B. Enzymes
C. Amino acids
D. Chromosomes

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Overview of Lecture

- Humans as hunks of protein
- DNA and protein synthesis
- Mitosis and Cancer
- Breast Cancer

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Gregor Mendel

Mendel had no idea about the existence or structure of DNA

- Genetics was born in **1866** when a monk named Gregor Mendel published a paper that defined the term "**gene**" as the unit that passes down heritable traits
- He argued that children inherited two copies of each gene
  - one copy from the mother
  - one copy from the father

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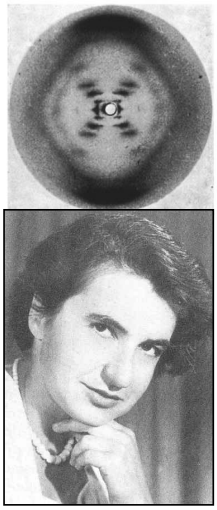
Discovery of DNA

James Watson & Francis Crick



Rosalind Franklin

- No one knew the structure of genes until the structure of DNA was discovered
- DNA Structure first described in the 1950s by:
  - Watson, Crick, Wilkins and Franklin

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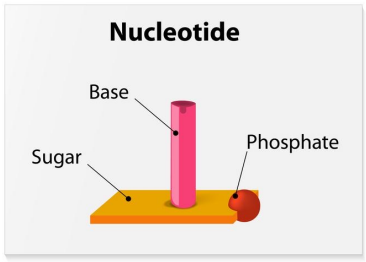
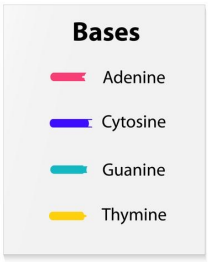
DNA Structure





- **Double Helix**
- **Four Nucleotides**
  - Each nucleotide consists of:
    - Sugar (S)
    - Phosphate (P)
    - **Base** (A,T,G or C).
- DNA consists of very long strands with millions of nucleotides in various sequences

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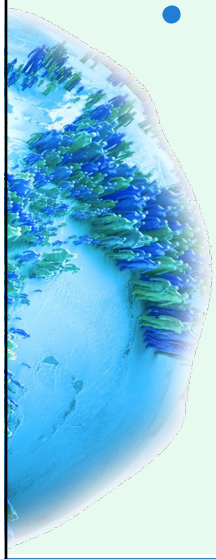
Why is each strand of DNA so long?



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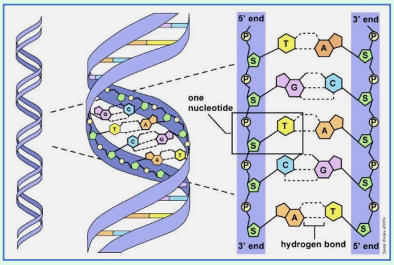
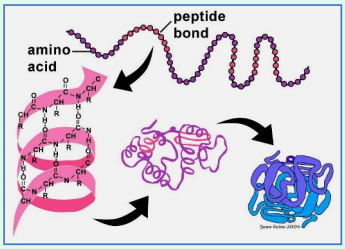
It takes a long sequence of DNA to code for the amino acids in all of the proteins





Answer:

- There are **2 million proteins**
- Each protein is **1000's of amino acids** long
- **DNA is 3 billion nucleotide bases** long
  - each letter [C,G,T,A] represents a nucleotide

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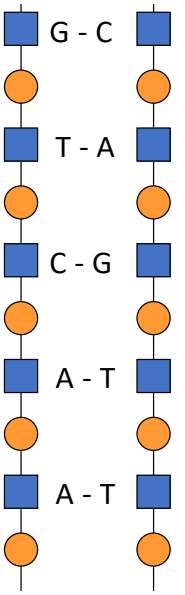
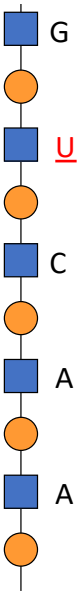
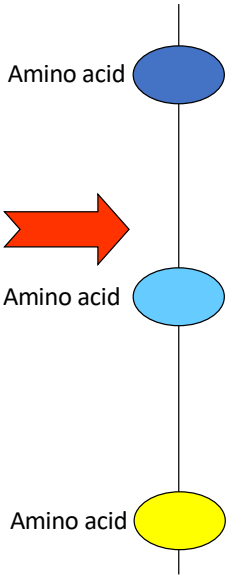
DNA contains a linear base sequence that…



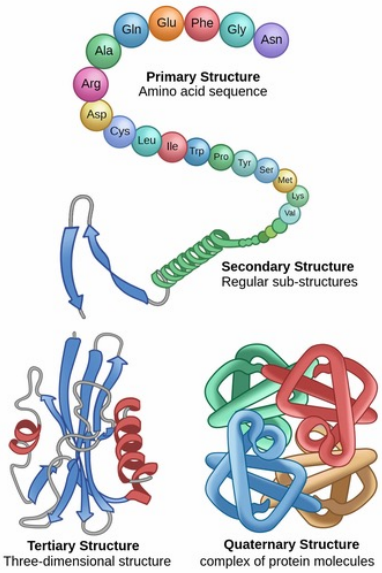
Is *transcribed* to RNA which…



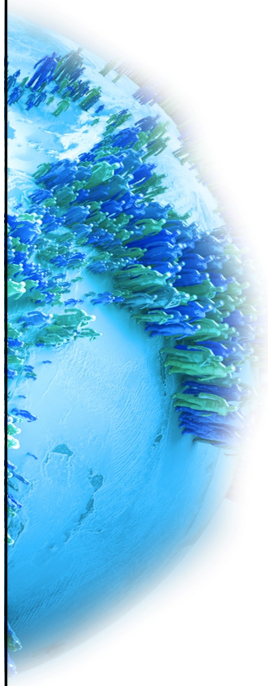
Translates into amino acid chains which...



Fold into Proteins



18

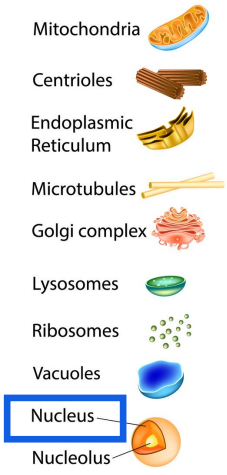


DNA is not a protein...

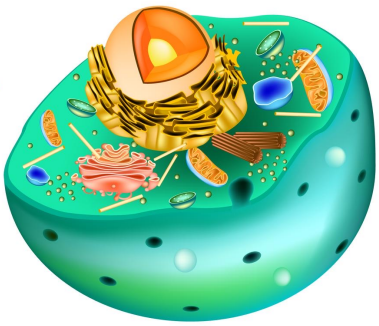
it is a molecule that contains the instructions for making proteins

19

Where is DNA located in the cell?



ANATOMY OF AN ANIMAL CELL



- The **nucleus**
- The nucleus contains chromosomes
  - Chromosomes are tightly wound chains of DNA
- Together, the 46 human chromosomes contain about 3 billion nucleotide bases.

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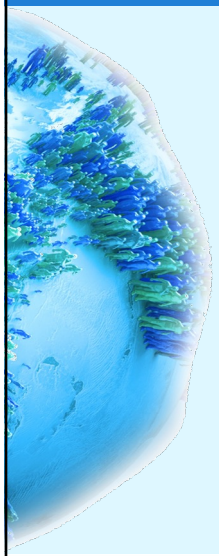
Overview of Lecture

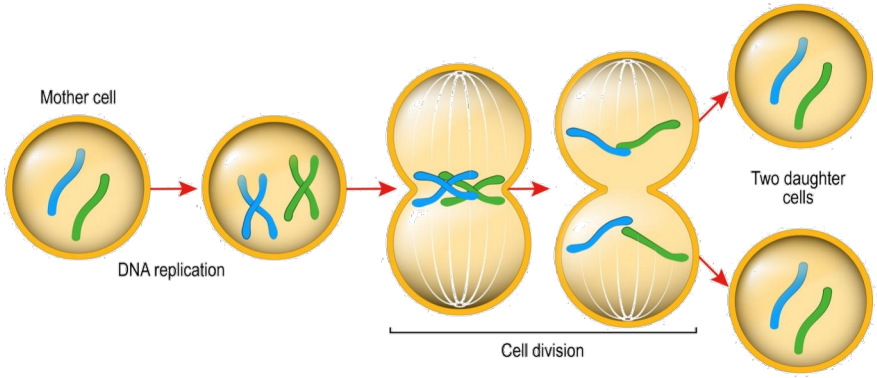


- Humans as hunks of protein
- DNA and protein synthesis
- Mitosis and Cancer
- Breast Cancer

21

Cell Division (Mitosis)

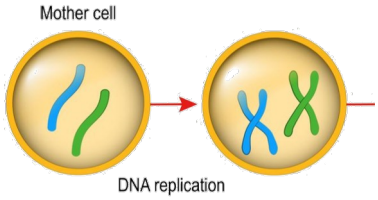
The growth of the organism itself and the repair of any damaged tissues are ensured by continuously dividing cells.



22

Cell Division (Mitosis)

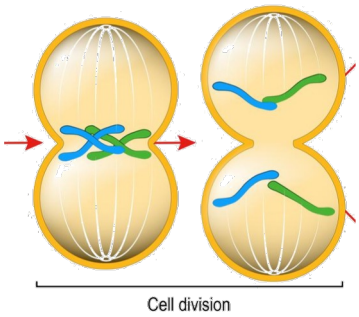
1. Before mitosis, the chromosomes are duplicated (**DNA Replication**) in order to make sure that each daughter cell will receive one copy of every chromosome.
(Here only 2 of the 23 chromosomes are shown.)



23

Cell Division (Mitosis)

2. During mitosis, the **duplicated chromosomes are distributed** to the two new cells which are formed by cell division.



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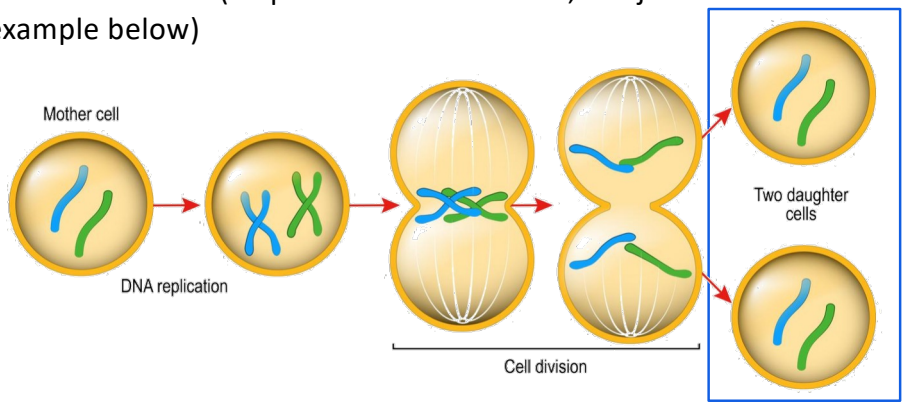
Cell Division (Mitosis)

3. After mitosis, there are **two new cells** with a complete complement of chromosomes (23 pairs of chromosomes, not just 2 as shown in the example below)



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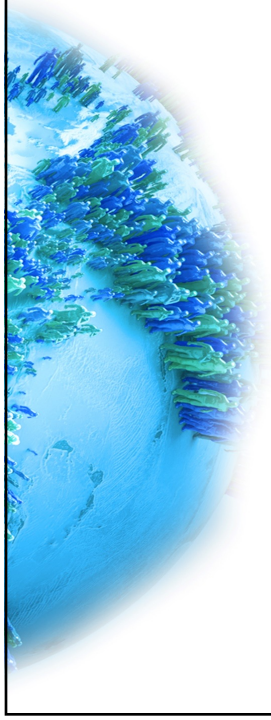


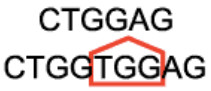
Cancer

results in uncontrolled mitosis caused by mutations in the DNA

26

Types of DNA Mutations

- Substitution: a mutation where one base is exchanged for another for another in the DNA



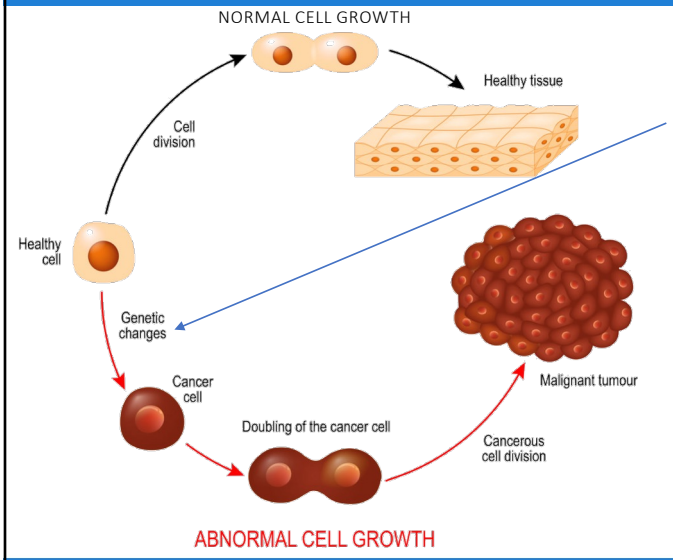
- Insertion: a mutation where extra bases are inserted into the DNA

- Deletion: a mutation where bases are eliminated from the DNA

Mutations

- **High-risk mutations** are those that disable an important error-free DNA repair process, thereby significantly increasing the person's risk of developing cancers
- Mutations can be **inherited** from either parent and may be passed on to both sons and daughters.

Cancer Formation



- Starts with mutation in DNA
- Mutations leads to uncontrolled mitosis
- Uncontrolled mitosis leads to tumor growth
- Tumors can spread (metastasize) to vital tissues or organs

29

Which statement about DNA is FALSE?

A. DNA is in the chromosomes.

B. DNA is made of millions of amino acids.

C. The structure of DNA was discovered by Watson, Crick, and others.

D. None of the above are false.

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Overview of Lecture

- Humans as hunks of protein
- DNA and protein synthesis
- Mitosis and Cancer
- Breast Cancer

31

Which statement about BRCA is FALSE?

A. BRCA genes produce proteins that help repair damaged DNA.

B. There are genetic tests for mutations in the BRCA gene.

C. If a person has a mutated version of the BRCA gene they can have an increased risk of developing breast cancer.

D. None of the above are false.

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Top 10 Cancers in Humans

	Common Types of Cancer	Estimated New Cases 2017	Estimated Deaths 2017
→	1. Breast Cancer (Female)	252,710	40,610
	2. Lung and Bronchus Cancer	222,500	155,870
	3. Prostate Cancer	161,360	26,730
	4. Colon and Rectum Cancer	135,430	50,260
	5. Melanoma of the Skin	87,110	9,730
	6. Bladder Cancer	79,030	16,870
	7. Non-Hodgkin Lymphoma	72,240	20,140
	8. Kidney and Renal Pelvis Cancer	63,990	14,400
	9. Leukemia	62,130	24,500
	10. Endometrial Cancer	61,380	10,920

Female breast cancer represents 15.0% of all new cancer cases in the U.S.

15.0%

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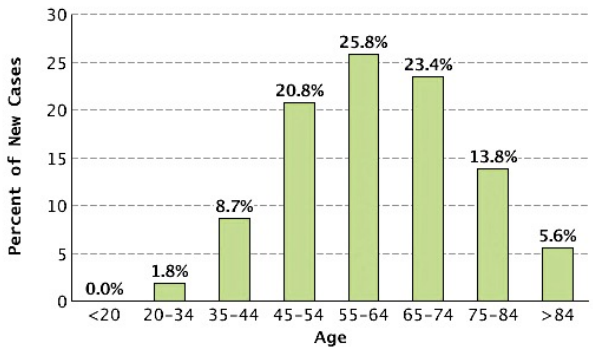
Age and Breast Cancer

Percent of New Cases by Age Group: Female Breast Cancer



SEER 18 2010-2014, All Races, Females

Female breast cancer is most frequently diagnosed among women aged 55-64.

Median Age At Diagnosis
62

- Most new cases of breast cancer occur in women older than 35
- The median age at diagnosis is 62.

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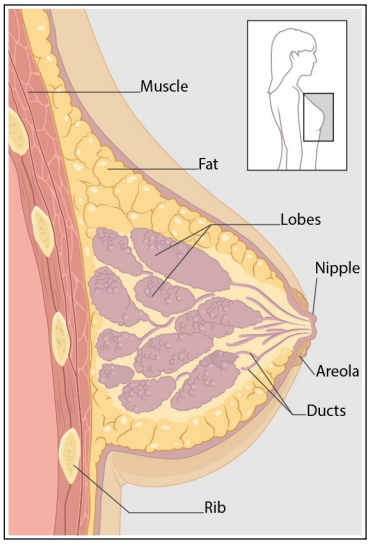
Female Breast Anatomy



- The female breast consists of fat deposits and milk producing lobes as well as the ducts that transport the milk to the nipple.
- Cancer can affect any of these tissues, resulting in different types of breast cancers

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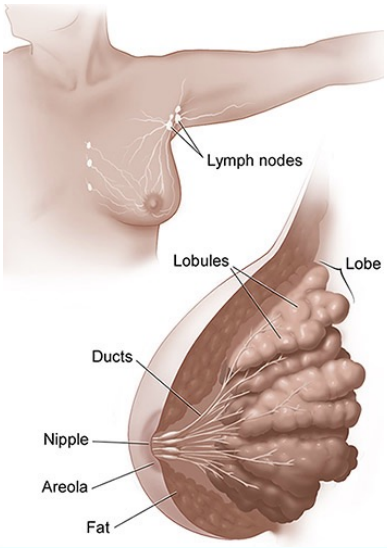
Cancer can spread to lymph nodes



- Cancerous cells can move from the breast into lymph nodes.
- Cancer can be spread (metastasize) to other parts of the body by movement through the lymphatic system

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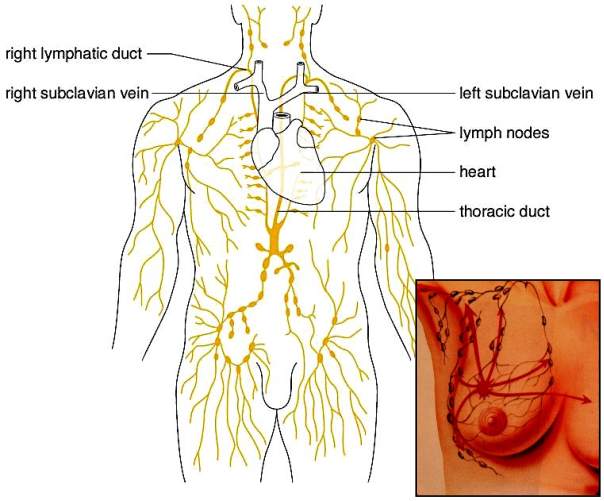
Lymphatic System



- Lymphatic vessels are responsible for returning body fluids from tissues throughout the body to the bloodstream.
- Lymphatic vessels occur throughout the body and can, therefore, carry cancer cells far from their point of origin (like the breast) and ultimately to the circulatory system.
- This can result in cancer spreading throughout the body

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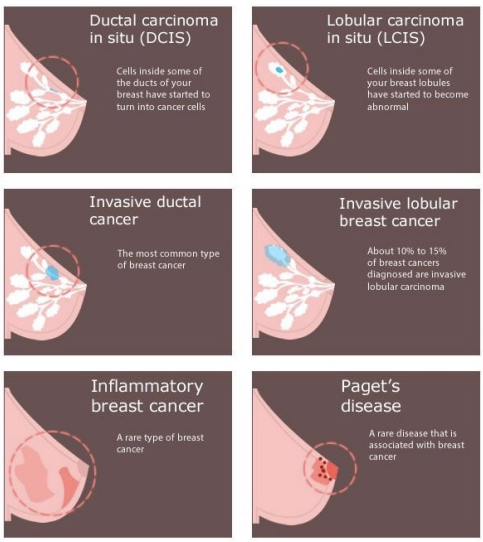
Types of Breast Cancer



- Cancer in different cells of the breast result in **different forms of Breast Cancer**
- You do not need to know all these specific forms of breast cancer... just that there *are* different forms.

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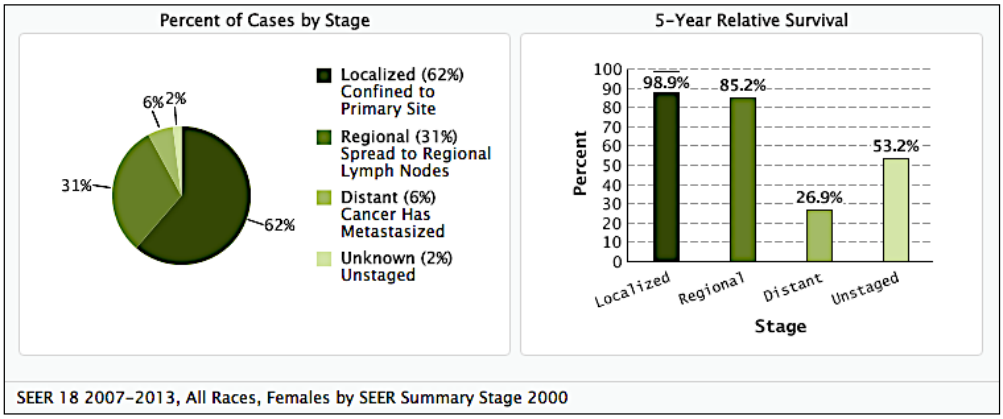
Survival is highest when cancer is detected before it spreads



Most breast cancers are detected in the **localized stage**, resulting in a **high survival rate**. Distant breast cancers in which the breast cancer has metastasized have a lower survival rate.

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Breast Self-Exam

Breast self-exam (BSE) is a step-by-step approach a woman can use to look at and feel her breasts.

However, BSE is not recommended as a screening tool for breast cancer.

Although it seemed promising when it was first introduced, studies have shown BSE does not offer the early detection and survival benefits of other screening tests [45].

A meta-analysis combined the results of the two largest randomized controlled trials on BSE. It compared women who did routine BSE to those who did not and found [45]:

- No difference in breast cancer survival
- Women who did BSE had more false positive results (which led to nearly twice as many biopsies with negative (no cancer found) results)

For more information about how to do a breast self-exam go to:
http://www.webmd.com/breast-cancer/guide/breast-self-exam#1

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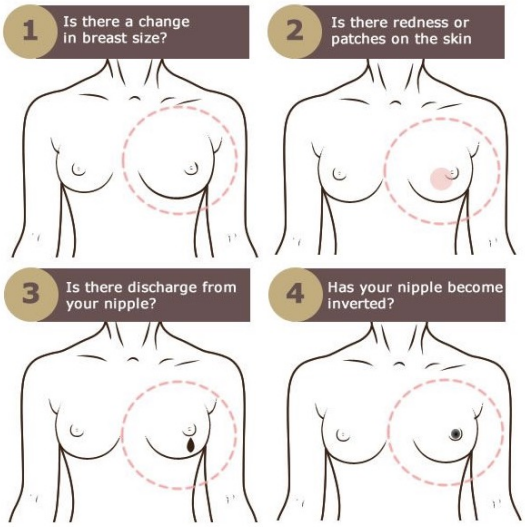
Symptoms of Breast Cancer



- Change in breast size
- Redness on the skin
- Discharge from nipple
- Inverted nipple

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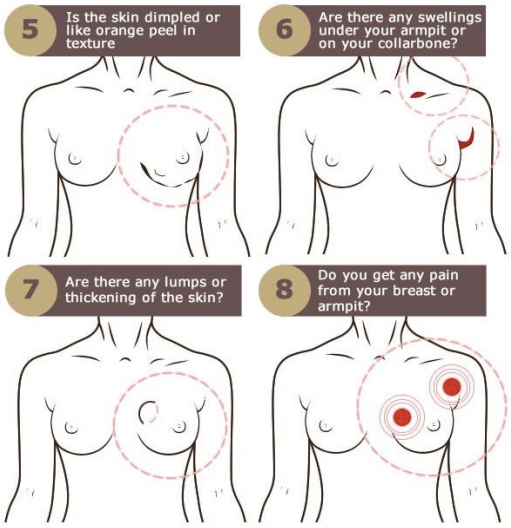
Symptoms of Breast Cancer (continued...)



- Skin dimpled (like orange peel)
- swellings under armpit or collarbone
- lumps or thickening of skin
- pain in breast or armpit

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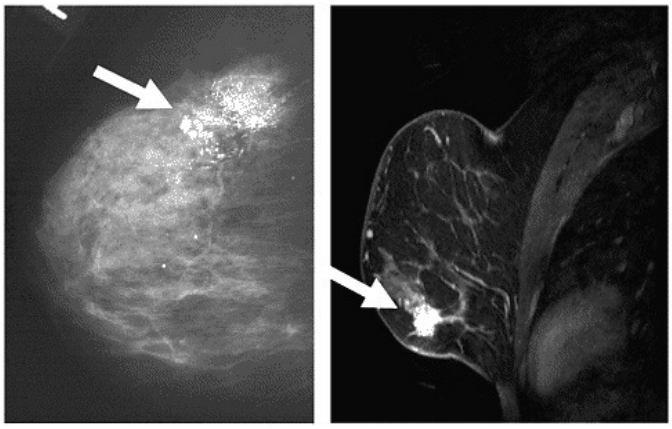
Mammograms



X-ray MRI

- Examples of MRI and x-ray images of two different cases of **DCIS**.
  - The case on the left is an **x-ray** mammogram of a breast showing DCIS in the upper portion of the breast.
  - The case on the right is an **MRI** mammogram showing DCIS in the lower portion.

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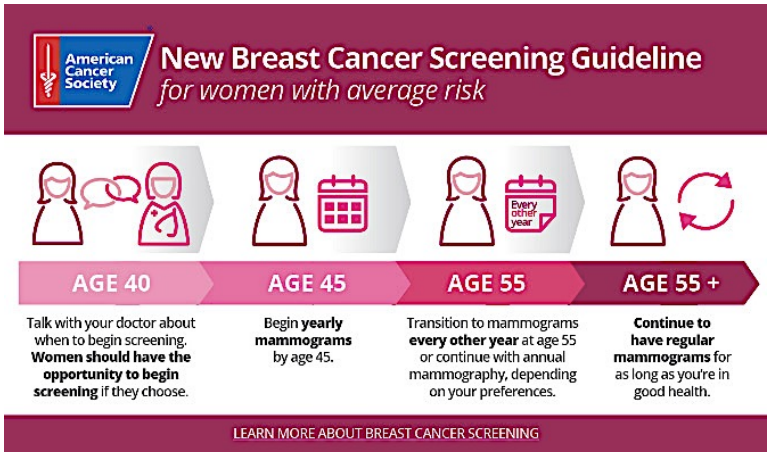
When to get a mammogram



- New research suggests some women may want to start getting yearly mammograms at age 40
- Talk to your doctor

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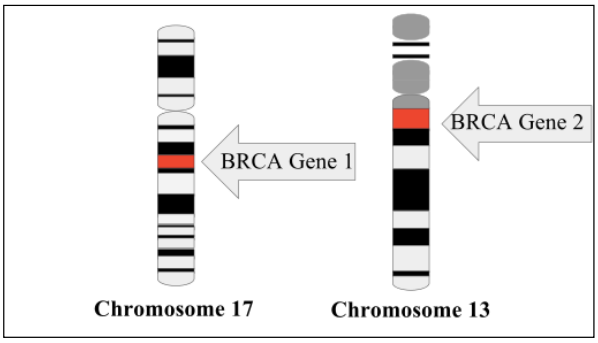
BRCA Genes



- The BRCA genes are tumor suppressor genes.
  - BRCA 1 is located on Chromosome 17
  - BRCA 2 is located on Chromosome 13.
- Both genes produce proteins that help repair damaged DNA, keeping the genetic material of the cell stable.
- A mutated BRCA gene can lead to increased risk of cancer, particularly breast or ovarian in women.

BRCA Mutations and Breast Cancer

- **No Mutation in BRCA genes**:
  - **12%** of females with the typical BRCA gene will develop breast cancer sometime during their lives.
- with **BRCA2 Mutation**:
  - **45%** of females will develop breast cancer by age 70
- with **BRCA1 Mutation**:
  - **55-65%** of females will develop breast cancer by age 70
- **Note**: simply having a mutated form of the BRCA gene does not automatically mean someone will get breast cancer... but there is an increased risk of developing breast cancer

BRCA Mutations and Ovarian Cancer

- **No Mutation in BRCA genes**:
  - **1.3%** of females with the typical BRCA gene will develop ovarian cancer sometime during their lives.
- with **BRCA2 Mutation**:
  - **11-17%** of females will develop ovarian cancer by age 70
- with **BRCA1 Mutation**:
  - **39%** of females will develop ovarian cancer by age 70
- **Note**: simply having a mutated form of the BRCA gene does not automatically mean someone will get ovarian cancer... but there is an increased risk of developing ovarian cancer

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Genetic Tests for BRCA Mutations

- Several different tests are available
  - those that look for a known mutation in one of the genes (i.e., a mutation that has already been identified in another family member)
  - and tests that check for all possible mutations in both genes.
- **DNA** (from a blood or saliva sample) is used for mutation testing.

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Prophylactic Surgery

- Surgery done before cancer is detected
- Females with mutated BRCA genes may choose to have both breasts removed (mastectomy) to reduce their risk of breast cancer.
- Surgery to remove a woman's ovaries and fallopian tubes can help reduce her risk of ovarian cancer.
  - Removing the ovaries also reduces the risk of breast cancer in premenopausal women by eliminating a source of hormones that can fuel the growth of some types of breast cancer.

Prophylactic Surgery

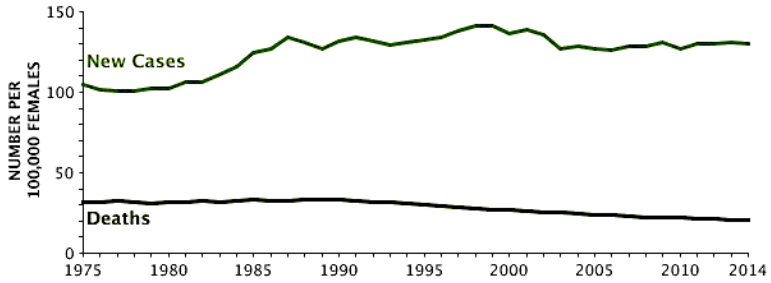
Angelina Jolie

- In May 2013, Angelina Jolie had both breasts and ovaries surgically removed after discovering she carries a mutation of the BRCA1 gene that dramatically increases her chance of having potentially fatal breast cancer and ovarian cancer.
- The mutation in her BRCA1 gene, left the mother-of-six with an estimated 87% risk of breast cancer and 50% risk of ovarian cancer.

New Cases and Deaths: Breast Cancer

New Cases, Deaths and 5-Year Relative Survival

View Data Table



Year	1975	1980	1985	1990	1995	2000	2005	2009
5-Year Relative Survival	75.2%	74.9%	78.4%	84.6%	86.8%	90.2%	90.5%	91.3%

SEER 9 Incidence & U.S. Mortality 1975-2014, All Races, Females. Rates are Age-Adjusted.

- New cases of breast cancer are much greater than deaths, showing that many women survive breast cancer.

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Next Lecture

Cloning and Individuality

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