

## Chapter 5

### Cancer: DNA Synthesis, Mitosis, and Meiosis

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### 5.1 What Is Cancer?

- \_\_\_\_\_ is the process through which a cell copies itself
- \_\_\_\_\_ begins when a cell divides although it should not
- Unregulated cell division leads to a \_\_\_\_\_, a mass of cells with no apparent function in the body

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### What Is Cancer?

- \_\_\_\_\_ tumors do not affect surrounding structures
- \_\_\_\_\_ tumors invade surrounding structures and are cancerous
- Malignant tumors can break away and start new cancers elsewhere through the process of \_\_\_\_\_

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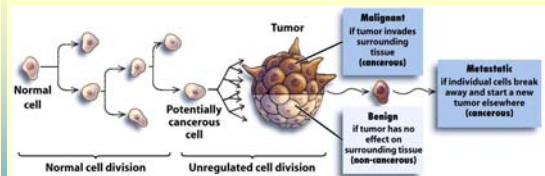


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### What Is Cancer?

- Cancer travels through the body by way of the lymphatic and circulatory systems
- The **lymphatic system** collects fluids lost from **capillaries**
- \_\_\_\_\_ are structures that filter lost fluids, called lymph

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### Lymphatic system

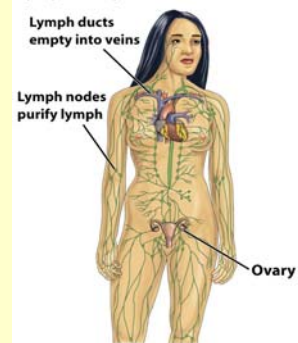


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## What Is Cancer?

- After they metastasize, cells gain access to the **circulatory system**, and the heart allow them to travel almost anywhere in the body

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## Cancer cells travel in lymph and blood

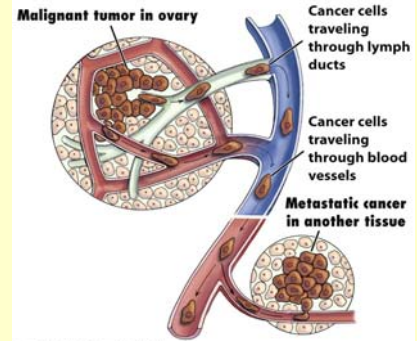


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## What Is Cancer?

- Cancer cells differ from normal cells:

- \_\_\_\_\_
- \_\_\_\_\_
- \_\_\_\_\_

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## What Is Cancer?

- All tissues that undergo cell division, such as ovarian tissue, are susceptible to cancer

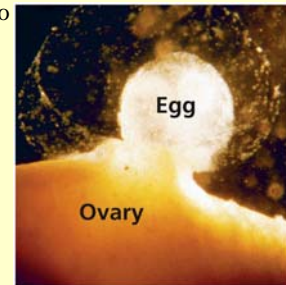


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## 5.2 Cell Division Overview

- Cell division produces new cells in order to:

- \_\_\_\_\_
- \_\_\_\_\_
- \_\_\_\_\_
- \_\_\_\_\_

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## Cell Division Overview

### Asexual reproduction:

- Make exact copies
- Does not need two parents
- Single celled organisms, like amoebas, carry out asexual reproduction

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### Cell Division Overview

- Some multicellular organisms carry out asexual reproduction
- Plants – grow from clippings

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### Cell Division Overview

- Before dividing, a copy of **DNA (deoxyribonucleic acid)** must first be made
- DNA is located within the nucleus and carries \_\_\_\_\_ – instructions for building the proteins that cells require

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### Cell Division Overview

- DNA is organized into structures called \_\_\_\_\_ which can carry hundreds of genes along their length
- The number of chromosomes in each cell depends on the organism: humans have 46
- DNA starts out in a string-like, uncondensed form (\_\_\_\_\_)

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### Uncondensed DNA

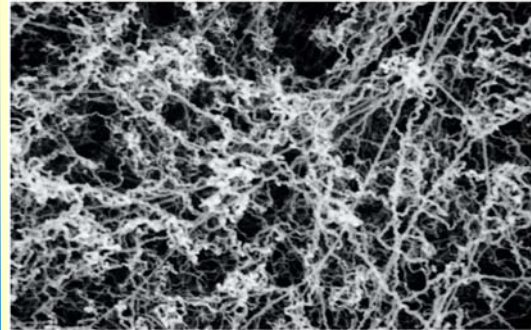


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### Cell Division Overview

- Before cell division, DNA is condensed into short, linear chromosomes
- When a chromosome is replicated during cell division, the copy carries the same genes
- Each chromosome is copied and the copy is called a \_\_\_\_\_
- The sister chromatid is connected to the original DNA by a \_\_\_\_\_

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### DNA condensed into chromosomes

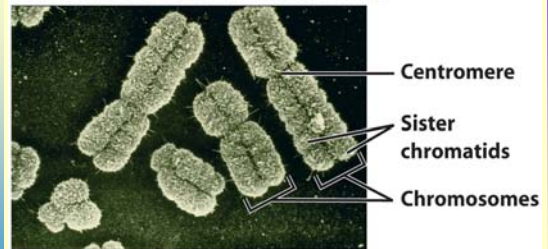


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### Cell Division Overview

- DNA is a double stranded molecule made of two single strands of nucleotides that are bonded together
- The DNA molecule looks a lot like a twisted rope ladder

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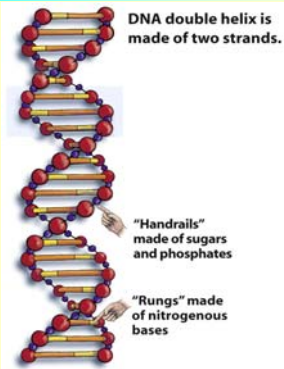


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### Cell Division Overview

- The "handrails" of the molecule are called the backbone which is made of sugars and phosphates
- The sugar and phosphate parts of the nucleotides are connected by covalent bonds

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### Cell Division Overview

- The "rungs" of the molecule are the bases:
  - A (\_\_\_\_\_)
  - T (\_\_\_\_\_)
  - G (\_\_\_\_\_)
  - C (\_\_\_\_\_)

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### Cell Division Overview

- The bases across the "ladder" are connected in a specific way:
  - A always bonds with T
  - C always bonds with G
- The connection is a hydrogen bond

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### Each strand is a chain of nucleotides.

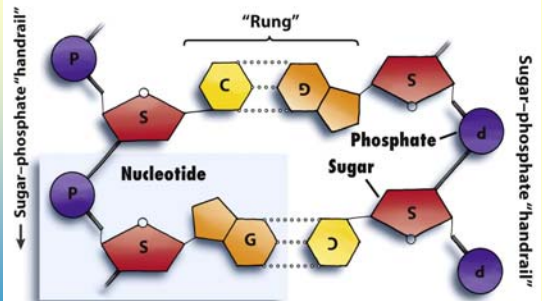
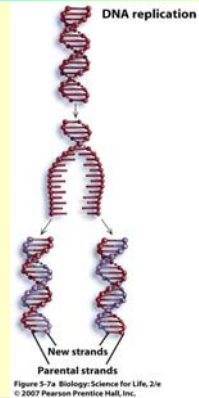


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## DNA Replication

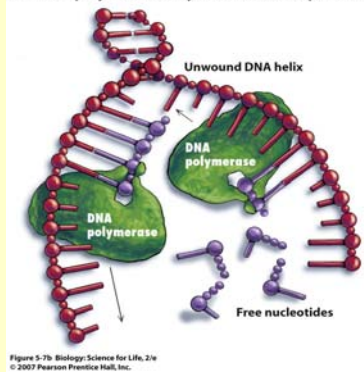
- DNA molecule separates at hydrogen bonds that hold bases together
- The enzyme \_\_\_\_\_ adds the correct base to the now single strand of DNA
- The covalent bond between sugars and phosphates is made

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## The DNA polymerase enzyme facilitates replication

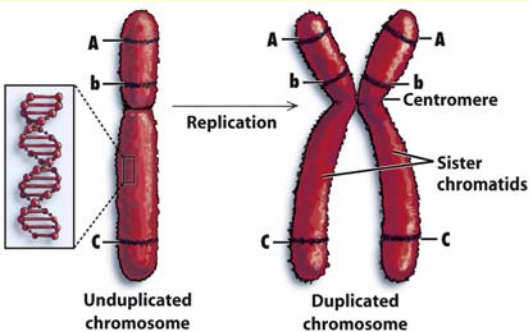


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## DNA Replication

- This results in two identical DNA molecules
- Each new DNA molecule is half new and half from the old molecule
- When an entire chromosome is copied, the two sister chromatids are connected at the centromere
- Now the cell is ready to divide

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## 5.3 The Cell Cycle and Mitosis

- **Mitosis** is an asexual division
- Is part of the **cell cycle** –
- Makes new cells that are exactly the same as the original cells

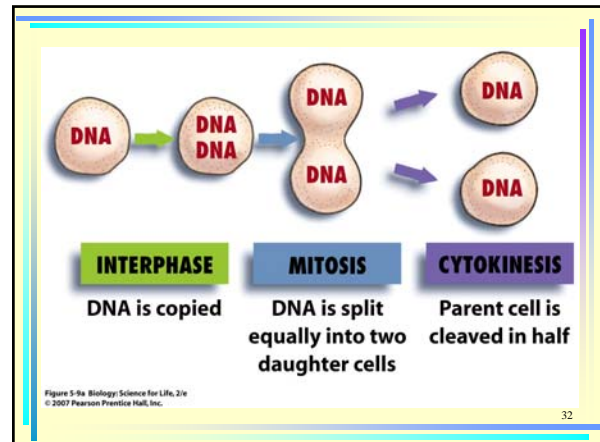
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## The Cell Cycle and Mitosis

For cells that divide by mitosis, there are 3 steps in the cell cycle:

1. \_\_\_\_\_
2. \_\_\_\_\_
3. \_\_\_\_\_

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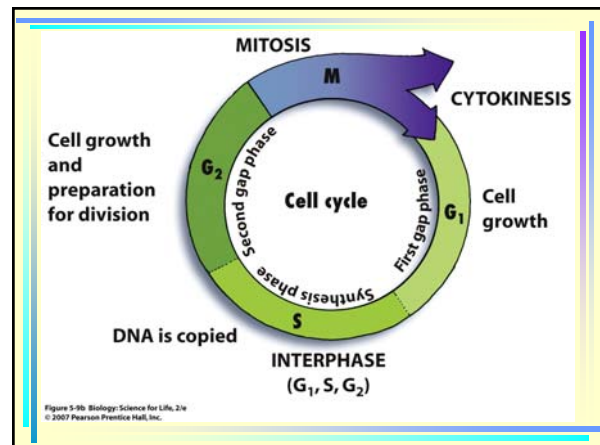
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## Interphase

- Most of a cell's life is spent in **interphase**
- Normal functions are carried out
- Three stages of interphase:

- \_\_\_\_\_
- \_\_\_\_\_
- \_\_\_\_\_

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## Interphase

- G<sub>1</sub>: first gap or growth phase
  - Organelles are duplicated
  - Cell gets larger
- S: synthesis phase
  - DNA is copied in this phase
  - Chromosomes are replicated
  - Get sister chromatids connected by centromeres
- G<sub>2</sub>: second gap phase
  - Synthesis of proteins necessary for mitosis

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## Mitosis

- The purpose of mitosis is to separate the sister chromatids so that each new cell has a complete set of chromosomes
- Steps of mitosis:

- \_\_\_\_\_
- \_\_\_\_\_
- \_\_\_\_\_
- \_\_\_\_\_

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## Mitosis

### Prophase:

- Replicated chromosomes condense
- **Microtubules** (spindle fibers) form at the **poles** (ends) of the cell
- The **nuclear envelope** disintegrates
- Microtubules attach to the centromeres of chromosomes

### Metaphase:

- Replicated chromosomes line up across equator of cell

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## Mitosis

### Anaphase:

- The centromere splits
- Microtubules pull sister chromatids apart towards poles

### Telophase:

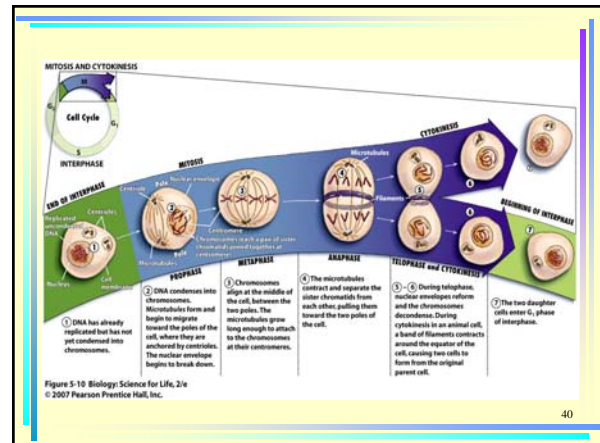
- **Nuclear envelopes** reform around chromosomes
- Chromosomes revert to uncondensed form

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## Cytokinesis

- The cell itself divides in half creating two identical daughter cells

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## Cytokinesis

For plant cells:

- Rigid **cell wall** prevents cell membrane from pinching in
- Prophase, metaphase, anaphase, and telophase similar to animal cells
- During cytokinesis, a \_\_\_\_\_ form from vesicles made of **cellulose** and proteins that will become a new cell wall

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## Cytokinesis

- Animal cells produce a band of filaments (proteins) that divide the cell in half (\_\_\_\_\_)
- The band of proteins contracts to pinch apart the 2 cells



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## Cytokinesis

- After cytokinesis, cells reenter the G<sub>1</sub> phase of interphase and repeat the cell cycle if the conditions are right
- Cells that go through the cell cycle in unfavorable conditions can lead to tumors

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## 5.4 Cell Cycle Control and Mutation

### Controls in the Cell Cycle

- \_\_\_\_\_ exist in the cell cycle
- Cell determines if cell is ready to enter next part of cell cycle

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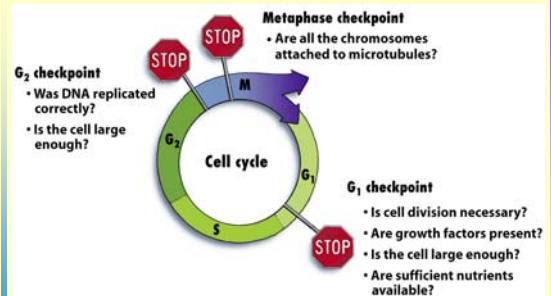


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### Controls in the Cell Cycle

- When the proteins that regulate the cell cycle don't work, the cell divides uncontrollably
- This results in a tumor

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### Controls in the Cell Cycle

- Mutations in the DNA can produce nonfunctioning proteins
- Mutations can be inherited or induced by exposure to \_\_\_\_\_ that damage DNA and chromosomes

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### Mutations to Cell-Cycle Control Genes

- Mutations in the DNA can produce nonfunctioning proteins
- Mutations can be in cell control proteins called \_\_\_\_\_

*proto-*: before  
*-onco*: cancer

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### Mutations to Cell-Cycle Control Genes

Proto-oncogenes:

- Normal genes on many different chromosomes
- Regulate cell division
- When mutated, they become \_\_\_\_\_

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### Mutations to Cell-Cycle Control Genes

- Many organisms have proto-oncogenes
- So many organisms can develop cancer



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### Mutations to Cell-Cycle Control Genes

- Proto-oncogenes carry instructions for building growth factors
  - Stimulate cell division only when the cellular environment is favorable and all conditions for division have been met
  - Cell division when needed
- Oncogenes overstimulate cell division

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### Mutations to proto-oncogenes

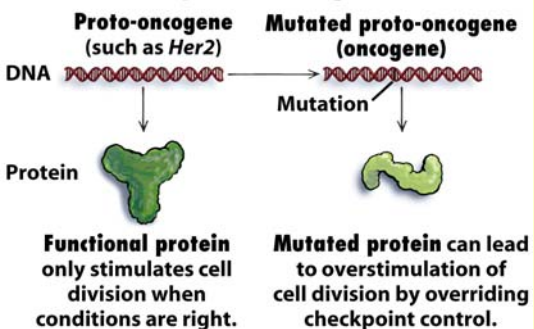
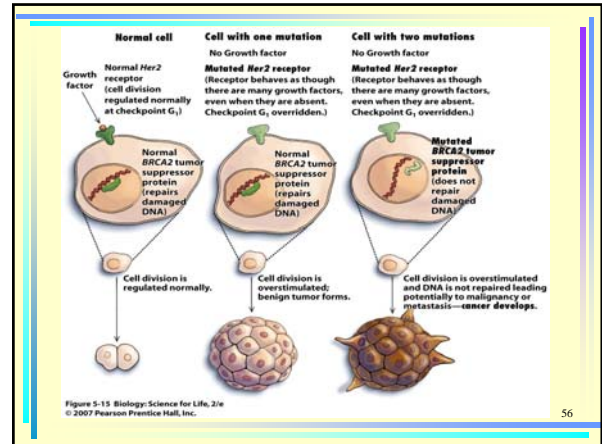
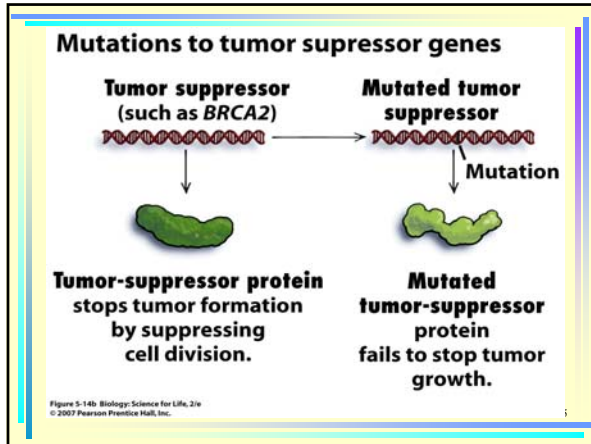


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### Mutations to Cell-Cycle Control Genes

- \_\_\_\_\_ are genes that carry instructions for producing proteins that stop cell division if necessary
- Suppressors are backup in case proto-oncogenes are mutated
- They can also be mutated
- Cells can then override the checkpoints

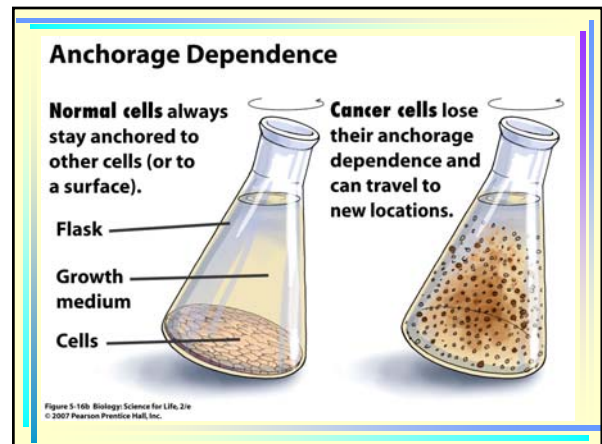
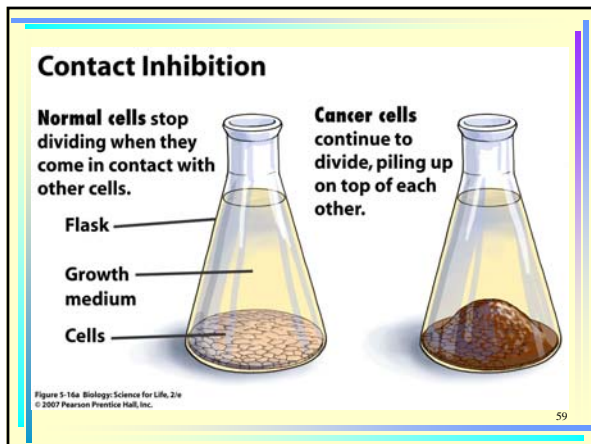


### From Benign to Malignant

➤ Some mutations that occur as a result of damaged DNA being allowed to undergo mitosis are responsible for the progression of a tumor from a benign state, to a malignant state, to metastasis

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- ### From Benign to Malignant
- **Angiogenesis** – growth of blood vessels caused by secretions from cancer cells
    - Increases the blood supply to cancer cells: more oxygen and nutrients
    - Cancer cells can divide more
    - Tumors develop, sometimes filling entire organs
  - **Contact inhibition** in normal cells prevents them from dividing all the time, which would force the new cells to pile up on each other
  - **Anchorage dependence** in normal cells keeps the cells in place
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### From Benign to Malignant

- Cancer cells divide too quickly and can leave the original site and enter the blood, lymph or tissues
- Most cells divide a set number (60-70) of times, then they stop dividing
- This usually limits benign tumors to small sizes
- Cancer cells can divide indefinitely, as they are **immortal** through the manipulation of the enzyme **telomerase**

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### Multiple Hit Model

- Multiple mutations are required for the development and progression of cancer
- **Multiple hit model** describes the process of cancer development
- Mutations can be inherited and/or can stem from environmental exposures
- Knowledge of cancer **risk factors** is important

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### 5.5 Cancer Detection and Treatment

- Earlier detection and treatment of cancer greatly increase the odds of survival
- Therefore, knowing the warning signs of cancer is important to health

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- C**hange in bowel or bladder habits
- A** sore that does not heal
- U**nusual bleeding or discharge
- T**hickening or lump
- I**ndigestion or difficulty swallowing
- O**bvious change in wart or mole
- N**agging cough or hoarseness

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### Detection Methods: Biopsy

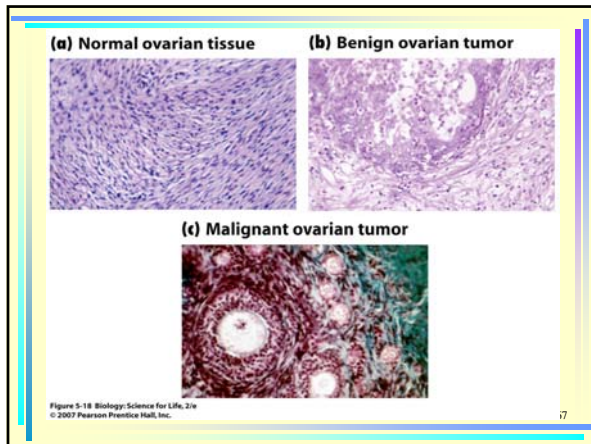
- Different cancers are detected by different methods
- Some cancers are detected by the excess production of proteins that are normally produced by a particular cell type
- When cancer is suspected, a **biopsy**, the surgical removal of cells, tissue, or fluid for analysis is performed
  - A needle biopsy is usually performed if the cancer is located on or close to the surface of the patient's body

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### Detection Methods: Biopsy

- Under a microscope, benign tumors appear orderly and resemble other cells in the same tissue
- Malignant tumors do not resemble normal tissue

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**Detection Methods: Biopsy**

- When possible, surgeons remove tumors with a \_\_\_\_\_ (thin tubular instrument inserted through a small abdominal incision and used to view organs in the pelvic cavity and abdomen)
  - Generally lead to quicker, easier recoveries
- Laparoscopic surgeries are possible only when growths are small
- Continued monitoring and treatment comes after surgery

**Treatment Methods: Chemotherapy**

- Chemicals that kill dividing cells are injected into the bloodstream during **chemotherapy**
- Combinations of chemical agents are used since cancer cells grow resistant
- Adverse effects on chemotherapy patients during treatment are numerous because normal cells that divide rapidly are also affected by chemotherapy treatments

**Treatment Methods: Chemotherapy**

- Hair follicles, cells that produce red blood cells, white blood cells, and cells that line the intestines and stomach are often damaged or destroyed causing
  - ✓ \_\_\_\_\_
  - ✓ \_\_\_\_\_ (dizziness and fatigue due to decreased numbers of red blood cells)
  - ✓ \_\_\_\_\_ due to decreases in number of white blood cells
  - ✓ \_\_\_\_\_
  - ✓ \_\_\_\_\_
  - ✓ \_\_\_\_\_

**Treatment Methods: Radiation**

- **Radiation therapy** uses high-energy particles to injure or destroy cells by damaging their DNA, making it impossible for these cells to continue to grow and divide
- It is often administered in addition to chemotherapy
- Typically involves a series of 10 to 20 treatments performed after the surgical removal of the tumor; sometimes radiation is used before surgery in order to decrease the size of the tumor

**Treatment Methods: Radiation**

- Radiation therapy is typically used only when cancers are located close to the surface of the body because it is difficult to focus a beam of radiation on internal organs
- A patient is in **remission** if the patient is no longer suffering negative impacts from cancer after a given period

## Essay 5.1 Cancer Risk Factors

- Known risk factors are linked to particular cancers...

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Cancer Location	Risk Factors	Detection	Comments
<b>Ovary</b> 	<ul style="list-style-type: none"> <li>Smoking</li> <li>Mutation to <i>BRCA2</i> gene</li> <li>Advanced age</li> <li>Oral contraceptive use and pregnancy decrease risk</li> </ul>	<ul style="list-style-type: none"> <li>Blood test for elevated CA125 level</li> <li>Gynecological exam</li> </ul>	<ul style="list-style-type: none"> <li>Fifth leading cause of death among women in the United States</li> </ul>
<b>Breast</b> 	<ul style="list-style-type: none"> <li>Smoking</li> <li>Mutation to <i>BRCA1</i> gene</li> <li>High-fat, low-fiber diet</li> <li>Use of oral contraceptives may slightly increase risk.</li> </ul>	<ul style="list-style-type: none"> <li>Monthly self exams, look and feel for lumps or changes in contour</li> <li>Mammogram</li> </ul>	<ul style="list-style-type: none"> <li>Only 5% of breast cancers are due to <i>BRCA1</i> mutations</li> <li>Second-highest cause of cancer-related deaths</li> <li>1% of breast cancer occurs in males</li> </ul>

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Cancer Location	Risk Factors	Detection	Comments
<b>Cervix</b> 	<ul style="list-style-type: none"> <li>Smoking</li> <li>Exposure to sexually transmitted Human Papilloma Virus (HPV)</li> </ul>	<ul style="list-style-type: none"> <li>Annual Pap-smear tests for the presence of pre-cancerous cells</li> </ul>	<ul style="list-style-type: none"> <li>Precancerous cells can be removed by laser surgery or cryotherapy (freezing) before they become cancerous.</li> </ul>
<b>Skin</b> 	<ul style="list-style-type: none"> <li>Smoking</li> <li>Fair skin</li> <li>Exposure to ultraviolet light from the sun or tanning beds</li> </ul>	<ul style="list-style-type: none"> <li>Monthly self-exams, look for growths that change in size or shape</li> </ul>	<ul style="list-style-type: none"> <li>Skin cancer is the most common of all cancers and is usually curable if caught early.</li> </ul>

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Cancer Location	Risk Factors	Detection	Comments
<b>Lung</b> 	<ul style="list-style-type: none"> <li>Smoking</li> <li>Exposure to second-hand smoke</li> <li>Asbestos inhalation</li> </ul>	<ul style="list-style-type: none"> <li>X-ray</li> </ul>	<ul style="list-style-type: none"> <li>Lung cancer is the most common cause of death from cancer, and the best prevention is to quit, or never start, smoking.</li> </ul>

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Cancer Location	Risk Factors	Detection	Comments
<b>Colon and rectum</b> 	<ul style="list-style-type: none"> <li>Smoking</li> <li>Polyps in the colon</li> <li>Advanced age</li> <li>High-fat, low-fiber diet</li> </ul>	<ul style="list-style-type: none"> <li>Change in bowel habit</li> <li>Colonoscopy is an examination of the rectum and colon using a lighted instrument.</li> </ul>	<ul style="list-style-type: none"> <li>Benign buds called polyps can grow in the colon; removal prevents them from mutating and becoming cancerous.</li> </ul>
<b>Prostate</b> 	<ul style="list-style-type: none"> <li>Smoking</li> <li>Advanced age</li> <li>High-fat, low-fiber diet</li> </ul>	<ul style="list-style-type: none"> <li>Blood test for elevated level of prostate specific antigen (PSA)</li> <li>Physical exam by physician, via rectum</li> </ul>	<ul style="list-style-type: none"> <li>More common in African-American men than Asian, white, or Native American men.</li> </ul>

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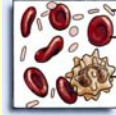
Cancer Location	Risk Factors	Detection	Comments
<b>Testicle</b> 	<ul style="list-style-type: none"> <li>Abnormal testicular development</li> </ul>	<ul style="list-style-type: none"> <li>Monthly self exam, inspect for lumps and changes in contour</li> </ul>	<ul style="list-style-type: none"> <li>Testicular cancer accounts for only 1% of all cancers in men, but is the most common form of cancer found in males between the ages of 15 and 35.</li> </ul>
<b>Blood (Leukemia)</b> 	<ul style="list-style-type: none"> <li>Exposure to high-energy radiation such as that produced by atomic bomb explosions in Japan during World War II</li> </ul>	<ul style="list-style-type: none"> <li>A sample of blood is examined under a microscope.</li> </ul>	<ul style="list-style-type: none"> <li>Cancerous white blood cells cannot fight infection efficiently; people with leukemia often succumb to infections.</li> </ul>

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## 5.6 Meiosis

- Another form of cell division, **meiosis**, occurs within \_\_\_\_\_, or sex organs
- Male gonads are \_\_\_\_\_ and female gonads are \_\_\_\_\_
- Meiosis produces sex cells – \_\_\_\_\_:
  - Male gametes: \_\_\_\_\_ cells
  - Female gametes: \_\_\_\_\_ cells

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## Meiosis

- Gametes have half the chromosomes (23) that \_\_\_\_\_ cells do (46)
- Meiosis reduces the number of chromosomes by one-half
- Fertilization of the male and female gamete will result in 46 chromosomes

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## Meiosis

- Which 23 chromosomes end up in a gamete?
  - One of each kind
- Chromosomes come in pairs
- Each somatic cell has two of every chromosome
- Each gamete has one chromosome from each homologous pair

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## Meiosis

- A \_\_\_\_\_ is a photograph of chromosomes in pairs
- The chromosomes have already been replicated and are in the shape of the letter X

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### Autosomes (22 pairs)



### Sex chromosomes (1 pair)



Female

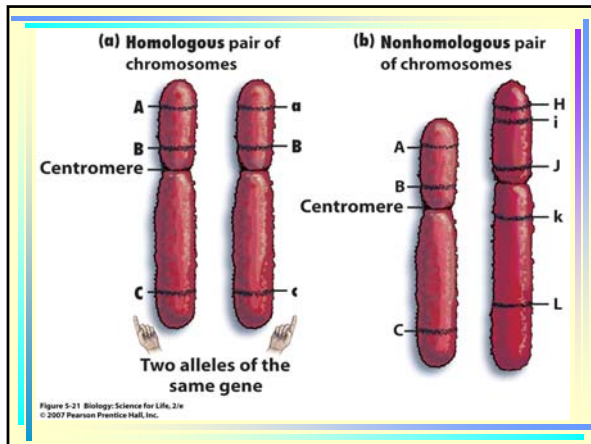
Male

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## Meiosis

- There are 22 pairs of \_\_\_\_\_ (non-sex chromosomes)
- There is one pair of sex chromosomes:
  - Males have one X and one Y chromosome
  - Females have two X chromosomes
- The pairs of chromosomes (\_\_\_\_\_ **pairs**) carry the same genes

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### Meiosis

Each homologous pair has the same genes

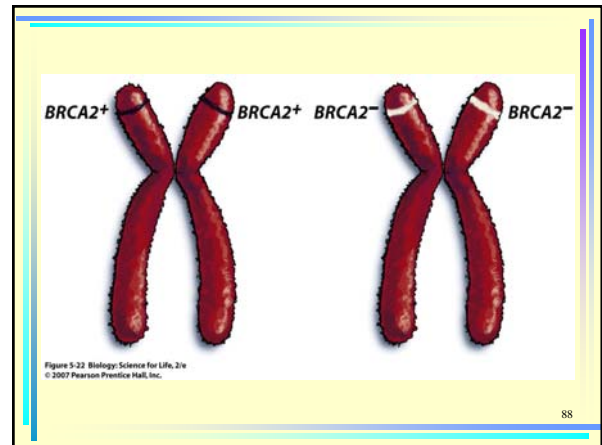
- Both chromosomes will have the genes on them in the exact same place
- Different versions of the same gene are called \_\_\_\_\_

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### Meiosis

- During the S phase of interphase, the DNA is copied and the homologous chromosomes consist of sister chromatids
- All four sister chromatids carry the same genes at the same locations, but not necessarily the exact same information

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### Meiosis

- During meiosis, the homologous pairs are separated, so each cell has only one of each pair
- This condition is called \_\_\_\_\_ ( $n$ ) – having only one of each kind of chromosome

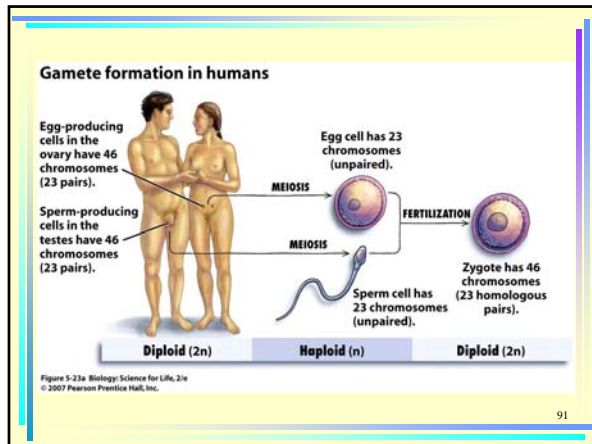
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### Meiosis

- Meiosis occurs in the sex cells in either the testes or ovaries (for humans) producing gametes
- When the sperm and egg fuse during fertilization, this produces a \_\_\_\_\_, or fertilized egg
  - This is \_\_\_\_\_ ( $2n$ ) – have two of each kind of chromosome

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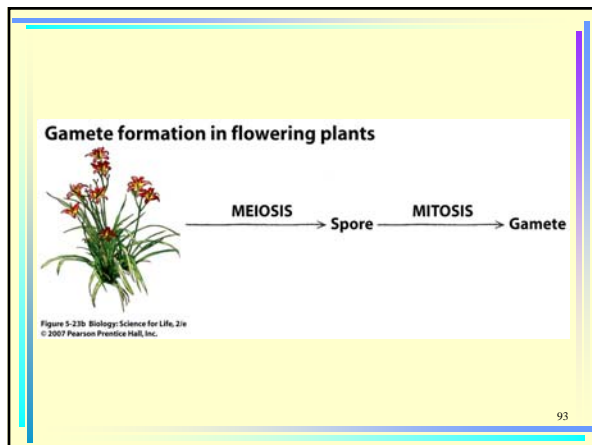




**Meiosis**

- Some eukaryotes produce gametes in a slightly different way
  - Flowering plants first undergo meiosis to produce spores and then mitosis to produce the actual gametes

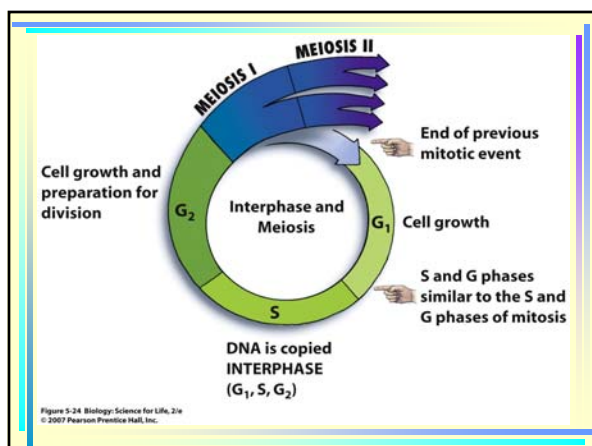
92



**Meiosis**

- Meiosis is preceded by interphase (G<sub>1</sub>, S, G<sub>2</sub>)
- Interphase is followed by 2 phases of meiosis
- Meiosis consists of phases:
  - Meiosis I, in which the homologous pairs are separated
  - Meiosis II, in which the sister chromatids are separated

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**Meiosis I**

There are four phases in meiosis I:

1. Prophase I – homologous pairs come together
2. Metaphase I – the homologous pairs line up at the equator...
3. Anaphase I – the homologous pairs separate
4. Telophase I – nuclear envelopes reform

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## Meiosis II

There are four phases in meiosis II:

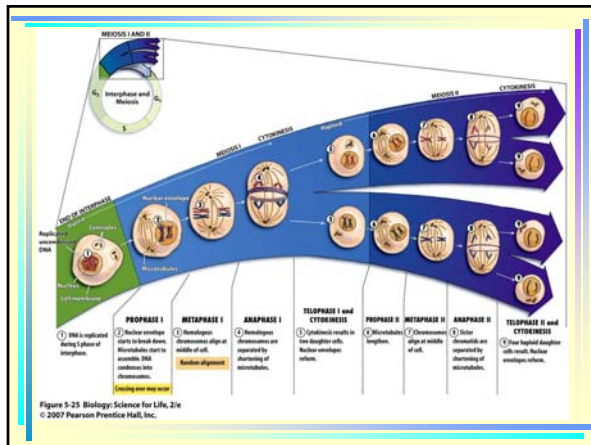
1. Prophase II – nuclear envelopes disappear
2. Metaphase II – chromosomes line up at equator
3. Anaphase II – sister chromatids separate
4. Telophase II – nuclear envelopes reform

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## Meiosis

- Since there are two separations, we end up with four cells
- Notice that the gametes are haploid – having one chromosome from each pair
- Each gamete carries half the genetic information as the parent

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## Crossing Over and Random Alignment

- There are millions of possible combinations of genes that each parent can produce because of:
  - Crossing over
  - Random alignment of homologous pairs

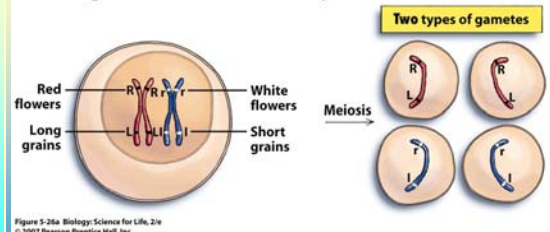
100

## Crossing Over

- When the homologous pairs are in prophase I of meiosis, they can exchange genetic information in the process of **crossing over**

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## If crossing over does not occur in Prophase I



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### If crossing over does occur in Prophase I

**Crossing over**

**Four types of gametes**

Meiosis

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### Random Alignment

- When the homologous pairs line up during metaphase I of meiosis, the way the homologs place themselves is **random alignment**
  - Members of a homologous pair line up randomly with respect to maternal or paternal origin during metaphase I of meiosis (thus increasing the genetic diversity of offspring)

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### One possible metaphase I alignment

**Two combinations of chromosomes in gametes**

1/2 normal gametes

1/2 gametes with two mutant alleles

Meiosis

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### Another possible metaphase I alignment

**Two additional combinations of chromosomes in gametes**

1/2 gametes with HER2 mutation

1/2 gametes with BRCA2 mutation

Meiosis

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### Mitosis and Meiosis

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- \_\_\_\_\_
- \_\_\_\_\_

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**Mitosis**

DNA replication

Prophase

Metaphase

Anaphase

Telophase

Two diploid daughter cells that are both genetically identical to the original parent cell.

**Meiosis I**

DNA replication

Prophase I

Metaphase I

Homologous chromosomes align as pairs.

Anaphase I

Telophase I

**Meiosis II**

(separates sister chromatids)

Daughter cells are haploid (have half as many chromosomes as the parent cell).

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