**Chapter 4**

**Cancer**

**DNA Synthesis, Mitosis, and Meiosis**

**What Is Cancer?**

* of cells with no function
* **Benign tumor**: doesn’t affect surrounding tissues
* **Malignant tumor**: invades surrounding tissues; **cancerous**
* **Metastasis**: cells break away from a malignant tumor and start a new cancer at another location
* Metastatic cells can travel throughout the body via the **circulatory system** or the **lymphatic system**.
  + Once in either system the cancer cells can travel anywhere in the body
* Cancer cells differ from normal cells:
  + Divide when they shouldn’t
  + Invade surrounding tissues
  + Move to other locations in the body
* **Risk factors**: increase a person’s risk of developing a disease
  + Tobacco use: tobacco contains many **carcinogens**
  + Alcohol consumption
  + High-fat, low-fiber diet
  + Lack of exercise
  + Obesity
  + Increasing age which weakens the immune system
  + Cells that divide frequently such as ovarian cells

**Passing Genes and Chromosomes to Daughter Cells**

* Asexual reproduction:
  + Only one parent
  + Offspring are genetically identical to parent
* Sexual reproduction
  + **Gametes** are combined from two parents
  + Offspring are genetically different from one another and from the parents
* Before dividing, cells must copy their **DNA**
* **Gene**: section of DNA that has the instructions for making all proteins
* One molecule of DNA is wrapped around proteins to form a **chromosome** containing hundreds of genes.
* Different species have different numbers of chromosomes (we have 46).
* Chromosomes are uncondensed before cell division
* Duplicated chromosomes, held together at the **centromere**, are called **sister chromatids**
* They are duplicated through **DNA replication**
* DNA molecule is a double stranded structure similar to a twisted ladder.
* The sides of the ladder are composed of a sugar-phosphate backbone.
* Nucleotides are connected to each other by hydrogen bonding to form the “rungs” of the ladder.
  + Adenine (A) pairs with thymine (T)
  + Cytosine (C) pairs with Guanine (G)
* DNA molecule is split up the middle of the helix
* Nucleotides are added to each side via hydrogen bonding
* Result is two identical daughter molecules, each with one parental strand and one new strand (**semiconservative replication**)
* **DNA polymerase**: the enzyme that replicates DNA
* It moves along the length of the unwound DNA and helps form the new strands

**The Cell Cycle and Mitosis**

* **Cell cycle** has three steps:
  + **Interphase**: the DNA replicates
  + **Mitosis**: the copied chromosomes are moved into daughter nuclei
    - Mitosis occurs in **somatic** or body cells.
  + **Cytokinesis**: the cell is split into 2 daughter cells

**Interphase**

* Interphase has three phases:
  + **G1**: cell grows, organelles duplicate
  + **S**: DNA replicates
  + **G2**: cell makes proteins needed to complete   
    mitosis
* Most of the cell cycle is spent in interphase

**Mitosis**

* Mitosis produces genetically-identical daughter nuclei
* Mitosis is followed by cytokinesis which splits the two nuclei into two daughter cells
* Four stages:
  + Prophase
  + Metaphase
  + Anaphase
  + Telophase
* **Prophase**:
  + Chromosomes condense
  + Nuclear envelope disappears
  + Microtubules pull the chromosomes around during cell division
    - Animal cells: microtubules attached to **centrioles** at the **poles** of the cell
* **Metaphase**:
  + Chromosomes are aligned across the middle of the cell by microtubules
* **Anaphase**:
  + centromeres split,
  + sister chromatids are pulled apart toward opposite poles
* **Telophase**:
  + Nuclear envelopes reform around chromosomes
  + Chromosomes revert to uncondensed form
* **Cytokinesis**
  + is the stage in which two daughter cells are formed from the original one
  + After cytokinesis, cells reenter interphase.
  + Animals:
    - Proteins pinch the original cell into two new cells
  + Plants:
    - Starts with vesicles forming the **cell plate.**
    - This results in a new **cell wall** being formed between the cells forming daughter cells.
      * The cell wall is made from **cellulose**

**Cell Cycle Control and Mutation**

* Cell division is a tightly controlled process
* Normal cells halt at **checkpoints**
* Proteins survey the condition of the cell
* Cell must pass the survey to proceed with cell division
* 3 checkpoints: G1,G2, and metaphase
* **Growth factors** stimulate cells to divide
* Growth factors bind to **receptors** to trigger a response from a cell
* **Mutation**: a change in the sequence of DNA
  + Changes to DNA can change the structure and function of the protein coded by the DNA
  + Mutations may be inherited or caused by carcinogens
* **Proto-oncogenes**: genes that code for the cell cycle control proteins
* When proto-oncogenes mutate, they become **oncogenes**
  + Their proteins no longer properly regulate cell division
  + They usually overstimulate cell division
* **Tumor suppressor genes**: genes for proteins that stop cell division if conditions are not favorable
  + When mutated, can allow cells to override checkpoints
* Depending on the number of mutations and whether the tumor suppressor protein is functional will determine whether it is a benign or malignant tumor that is formed.

**Cancer Development Requires Many Mutations**

* Progression from benign tumor to cancer requires many mutations.
* **Angiogenesis**: tumor gets its own blood supply
* Loss of **contact inhibition**: cells will now pile up on each other
* Loss of **anchorage dependence**: enables a cancer cell to move to another location
* **Immortalized**: cells no longer have a fixed number of cell divisions due to an enzyme called **telomerase**

**Cell Cycle Control and Mutation – Multiple Hit Model**

* **Multiple hit model**: process of cancer development requires multiple mutations
* Some mutations may be inherited (familial risk)
* Most are probably acquired during a person’s lifetime

**Cancer Detection and Treatment**

* Early detection increases odds of survival
* There are different detection methods for different cancers
* Some cancers produce increased amount of a characteristic protein
* **Biopsy**: surgical removal of cells or fluid for analysis
  + **Needle biopsy**: removal is made using a needle
  + **Laparoscope**: surgical instrument with a light, camera, and small scalpel
* **Chemotherapy**: drugs that selectively kill dividing cells
  + Combination of different drugs used (“cocktail”)
  + Interrupt cell division in different ways
  + Helps prevent resistance to the drugs from arising
  + Normal dividing cells are also killed (hair follicles, bone marrow, stomach lining)
* **Radiation therapy**: use of high-energy particles to destroy cancer cells
  + Damages their DNA so they can’t continue to divide or grow
  + Usually used on cancers close to the surface
  + Typically performed after surgical removal of tumor
* If a person remains cancer free after treatment for 5 years they are in **remission** and after 10 years they are cured.

**Meiosis**

* Specialized form of cell division in **gonads** to produce **gametes**
* Reduces number of chromosomes in each cell by one-half
  + Chromosomes come in **homologous pairs**
  + Gamete gets one of each pair
* Chromosomes can be visualized using a **karyotype**.
  + Human **somatic cells** have 22 pairs of **autosomes** and one pair of **sex chromosomes**
* Gametes are **haploid** or have 1 set of 23 chromosomes
* When the egg and sperm nuclei fuse it forms a zygote which is **diploid**
* Somatic or body cells are also **diploid**
* Starts with interphase – DNA is duplicated
* Meiosis takes place in two stages:
* **Meiosis I**
  + Separating out the homologous pairs into 2 separate cells
* **Meiosis II**

Separating out the sister chromatids in each cell to produce 4 haploid cells

* **Crossing over**: exchange of equivalent portions of chromosomes between members of a homologous pair
  + Results in new types of gametes being formed
  + **Linked genes** typically cross over together
* **Random alignment**: the way in which different pairs of chromosomes align and get separated during meiosis I is random
  + Results in different types of games being formed
* **Nondisjunction**: failure of homologues to separate normally during meiosis
  + Results in a gamete having one too many chromosomes (**trisomy**) or one too few chromosomes (**monosomy**)
  + Most embryos that result from such gametes will die before birth
  + Several chromosome abnormalities are known in humans (Table 6.2)
* For cancer mutations to be passed on to offspring, they must take place in cells that give rise to gametes.
* Mutations caused by environmental exposures are not passed on unless the mutation occurs in the gametes.
  + Mutations in somatic cells (e.g., skin cancer from UV ray exposure) are not heritable.