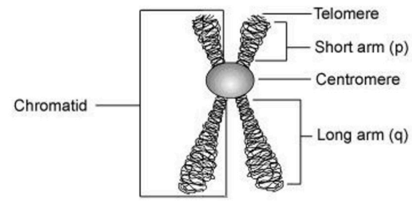
Name: ________________

Chapter 9: DNA Structure and Function

Chromosome Structure



- Class Introduction
    - DNA - polymer of nucleic acid; double stranded in a helix shape
        - 1' binds to the base
        - 5' binds to the phosphate
        - 3' binds to the next nucleotide
    - Chromosomes - physical division of the genome
        - 100s or 10000s of genes on a chromosome
        - Humans get 23 diploid pairs from each parent, totalling 46
        - Chromosome 1 is the largest, 46 is the smallest
        - 1-22 are autosomal (chromosome that is not a sex chromosome)
        - 23 is the sex chromosome (a chromosome involved with determining the sex of an organism)
    - Alles - one of two or more alternative forms of a gene that arise by mutation and are found at the same place on a chromosome
        - Different mutations but the same gene in the same position
        - Notation: C_{1M} (maternal) and C_{1P} (paternal)
- 9.1a: Genomic DNA
    - Genome - the complete set of genes or genetic material present in a cell or organism
        - Eukaryotic Genome - a cell's DNA packaged as a double-stranded DNA molecule
            - Chromosome count varies between organisms
                - Human body cells have 23; gametes have 23 each
                - Gamete - **hap**loid reproductive cell or sex cell (sperm or egg)
            - **Dip**loid - cell, nucleus, or organism containing two sets of chromosomes (2*n*)
            - **Hap**loid - cell, nucleus, or organism containing one set of chromosomes (*n*)
                - *n* represents a single set of chromosomes
        - Prokaryotic Genome - a cell's DNA packaged as a single, double stranded DNA molecule shaped like a circle or loop
            - Some prokaryotes also have smaller loops of DNA called plasmids that are not essential for normal growth
            - Bacteria can exchange plasmids with other bacteria; may get beneficial new genes that the recipient can add to their chromosomal DNA
    - Genetic material is housed in the nucleoid
    - Genes - physical and functional unit of heredity, a sequence of DNA that codes for a protein)
    - Locus - the position of a gene on a chromosome
    - Chromosome - structure in all living cells that consists of a single molecule of DNA bonded to various proteins and that carries the genes determining heredity; condensed chromatin
        - Homologous Chromosomes - chromosomes of the same morphology with genes in the same location; **dip**loid organisms have pairs of homologous chromosomes (homologs), with each homolog derived from a different parent
            - Have the same genes in the same locus
            - Each pair of chromosomes comes from a different parent; genes themselves aren't identical
            - *Variation of individuals* within a species is due to the specific combination of genes inherited from both parents
                - Slight variation can result in alternative traits
- 9.1b: Eukaryotic Chromosomal Structure and Compaction
    - DNA itself is very expansive, so it must be tightly packed to fit in a cell but still accessible
    - During some stages of the cell cycle, the long strands of DNA are condensed into compact chromosomes
        - *First Level of Compaction*: short stretches of the DNA double helix wrap around a core of eight histone proteins are regular intervals along the entire chromosome's length

- The DNA-histone structure is called <u>chromatin</u>
- <u>Histone Proteins</u> - proteins found in the chromatin of all eukaryotic cells; associated with DNA to form nucleosomes
- <u>Nucleosome</u> - subunit of chromatin composed of a short length of DNA wrapped around a core of histone proteins
- <u>Linker DNA</u> - DNA connecting the nucleosome
- A DNA molecule in this form is about 7 times shorter than the double helix without the histones, and the beads are about 10 nm in diameter, in contrast with the 2-nm diameter of a DNA double helix

■ *Second Level of Compaction*: nucleosomes and linker DNA are coiled into 30nm chromatin fiber
- Coiling shortens the chromosome to about 50 times smaller than the original size

■ *Third Level of Compaction*: fibrous proteins are used to pack the chromatin
- Fibrous proteins also ensure that each chromosome in a nondividing cell occupies a certain area in the nucleus that doesn;t overlap with any of chromosomes

➢ Recent research shows that while histones are required for tightly packing each chromosome, they are not required for its specific structure
- ■ <u>Condensin proteins</u> are used to generate structure

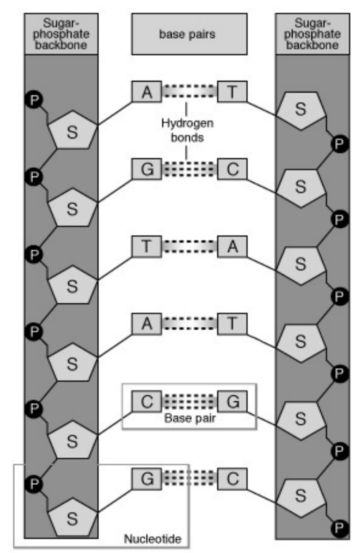
➢ DNA and Replication
- ■ <u>Chromatid</u> - single DNA molecule of two strands of duplicated DNA and associated proteins held together at the centromere
- ■ When fully compact, the pairs are bound by cohesion proteins
  - <u>Centromere</u> - region at which sister chromatids are bound together; a constricted area in condensed chromosomes

DNA Structure and Sequencing

❖ 9.2 Introduction

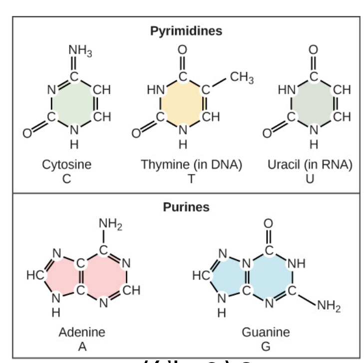
➢ The monomers of DNA are nucleotides

➢ <u>Nucleotides</u> - deoxyribose (5-C sugar), a phosphate group and a nitrogenous base; held together by covalent bonds in one strang (strands are held together by hydrogen bonds)
- ■ Nitrogenous Bases
  - Adenosine (A) and Thymine (T)
  - Guanine (G) and Cytosine (C)
- ■ Adenine and guanine are *purines*; cytosine and thymine are *pyrimidines*
- ■ Nucleotides combine by *covalent* bonds called <u>phosphodiester bonds</u>/<u>linkages</u>



➢ Purines and Pyrimidines
- ■ <u>Purines</u> - have a double ring structure with a 6-ring fused to a 5-ring
- ■ <u>Pyrimidines</u> - have a single 6-membered ring structure; smaller sized

➢ Nucleotide Structure
- ■ The carbon atoms are numbered 1', 2', 3', 4', and 5'
- ■ Phosphate group attaches to the hydroxyl group of 3’ carbon sugar of the next nucleotide, forming a 5’-3’ phosphodiester bond



➢ DNA is <u>antiparallel</u>, meaning one strand is in the 5' to 3' direction and the other is oriented in the 3' to 5' direction

❖ 9.2a: DNA Sequencing Techniques

➢ Used to be very expensive and long process
- ■ Using radiolabeled nucleotides also compounded the problem through safety concerns

Name: ________________

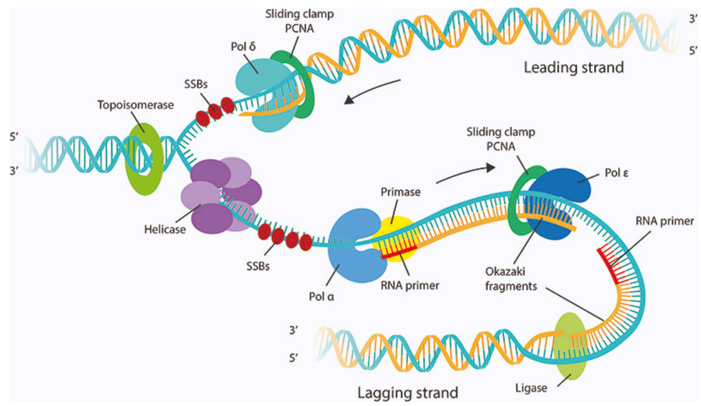
- ➢ Today's technology allows cheaper, safer, and quicker results
- ➢ *Fred Sanger* developed the sequencing method used for the human genome sequencing project, which is widely used today

DNA Replication in Prokaryotes

- ❖ DNA Replication - process of a cell making an additional copy of all of its DNA
    - ➢ Has been very well studied in prokaryotes due to the small size of the genome
    - ➢ Employs a large number of proteins and enzymes
        - ■ DNA Polymerase - replicates DNA by adding nucleotides one by one to the DNA chain
            - Gets energy to add nucleotides from nucleotides that have 3 phosphates: ATP, GTP, TTP, and CTP
            - The energy released from broken phosphodiester bonds; used to form the phosphodiester bond between the incoming nucleotide and the growing chain
            - Three types of polymerases: DNA pol I, DNA pol II, and DNA pol III
        - ■ Helicase - helps to open up the DNA helix by breaking the hydrogen bonds
        - ■ Single-Stranded Binding Proteins - binds to the single-stranded DNA; helps in keeping the two strands of DNA apart so they may serve as templates
        - ■ Primase - synthesizes the RNA primer; the primer is needed for DNA pol to start synthesis of a new DNA strand
        - ■ Topoisomerase - enzyme that causes underwinding or overwinding of DNA when DNA replication is taking place
        - ■ Ligase - enzyme that catalyzes the formation of a phosphodiester linkage between the 3' OH and 5' phosphate ends of the DNA
    - ➢ Anatomy
        - ■ Origin - specific nucleotide sequences of replication where replication begins
        - ■ Replication Forks - Y-shaped structure formed during initiation of replication
        - ■ Primer - short stretch of nucleotides that is required to initiate replication; in the case of replication, the primer has RNA nucleotides
        - ■ Leading Strand - strand that is synthesized continuously in the 5'-3' direction which is synthesized in the direction of the replication fork
        - ■ Okazaki Fragments - DNA fragment synthesized in short stretches on the lagging strand
        - ■ Lagging Strand - during replication, the strand that is replicated in short fragments and away from the replication fork
        - ■ Sliding Clamp - ring-shaped protein that holds the DNA pol on the DNA strand
- ❖ The Process of DNA Replication
    1. *Origins* signal where to begin replication
    2. The origin is recognized by *helicase* which begins to unwind the DNA by breaking the hydrogen bonds between the nitrogenous base pairs
    3. Two *replication forks* are formed at the origin of replication and these get extended bi- directionally as replication proceeds
    4. *Single-strand binding proteins* coat the single strands of DNA near the replication fork to prevent the single-stranded DNA from winding back into a double helix
    5. *DNA polymerase* begins to add nucleotides in only the 5' to 3' direction
        - It also requires a free 3'-OH group to which it can add nucleotides by forming a phosphodiester bond between the 3'-OH end and the 5' phosphate of the next nucleotide
        - This essentially means that it cannot add nucleotides if a free 3'-OH group is not available
    6. A *primer* provides a free 3' OH end
        - *RNA primase* synthesizes an RNA primer, about five to ten nucleotides long and complementary to the DNA
        - Because this sequence primes the DNA synthesis, it is appropriately called the primer
    7. Due to the antiparallel nature of DNA, the replication of the leading strand proceeds in one sweep; but the lagging strand is replicated in *Okazaki fragments*
        - Each requires a primer for synthesis
    8. A *sliding clamp* holds the DNA polymerase in place as it adds nucleotides

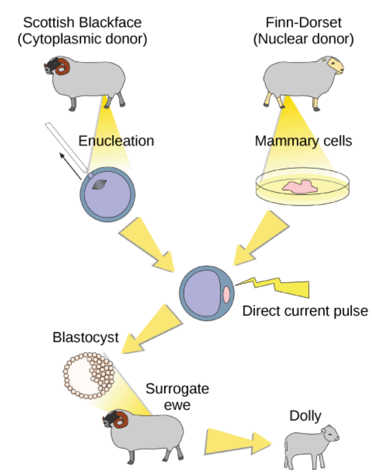
Name: ________________

9. *Topoisomerase* prevents the over-winding of the DNA double helix ahead of the replication fork as the DNA is opening up
    - Causes temporary nicks in the DNA helix and then reseals it
10. As synthesis proceeds, the RNA primers are replaced by DNA
11. *Ligase* seals the nicks that remain between the newly synthesized DNA and the previously synthesized DNA



- ❖ Replication Isn't Perfect
    - ➢ The DNA polymerase sometimes makes mistakes
        - ■ DNA polymerase has a proof-reading ability to check its own work and different types of repair processes exist to fix different kinds of mutations
    - ➢ However, not every mistake is fixed; mistakes left unchecked are called mutations
        - ■ Mutations - passed on because a cell can only fix a mistake as soon as it happens, so if it's not fixed right away, it stays in the cell's DNA permanently
- ❖ DNA Editing
    - ➢ Ligase removes all primers and replaces them with nucleotides
    - ➢ DNA polymerase proofreads accidentally incorporated nucleotides and replaces them
        - ■ Bulge - sequence with the wrong nucleotide
        - ■ DNA polymerase doesn't know which is the wrong one; results in a mutation

Cloning



- ❖ 9.4a: Molecular Cloning - cloning of DNA fragments
    - ➢ Reproductive Cloning - the re-creation of a whole organism
    - ➢ Twinning - cells are separated from a blastocyst; both groups of cells continue replicating to form 2 identical individuals
- ❖ 9.4b: Cellular Cloning - production of identical cell populations by binary fission
    - ➢ Unicellular organisms, such as bacteria and yeast, naturally produce clones as their form of reproduction
    - ➢ Pathenogenesis - "virgin birth"; occurs when an embryo grows and develops without the fertilization of the egg occurring; asexual reproduction
    - ➢ Most multicellular organisms reproduce in a genetic hybridization of two parents (sexual reproduction)
        - ■ Sexual reproduction requires 2 cells: **hap**loid egg and sperm
            - When the egg and sperm fuse, it creases a **dip**loid zygote
            - The zygote nucleus contains the genetic information to produce a new individual
            - However, early embryonic development requires the cytoplasmic material contained in the egg cell
            - This idea forms the basis for reproductive cloning
                - ◆ If the **hap**loid nucleus of an egg cell is replaced with a **dip**loid nucleus from the cell of any individual of the same species (called a donor), it will become a zygote that is genetically identical to the donor
                - ◆ Somatic Cell Nuclear Transfer - transfer of a somatic (body) cell's nucleus into an egg cell missing its own nucleus
    - ➢ The First Cloned Animal: Dolly the Sheep
        - ■ The success rate of reproductive cloning at the time was very low

        - Dolly lived for seven years and died of respiratory complications
        - There is speculation that because the cell DNA belongs to an older individual, the age of the DNA may affect the life expectancy of a cloned individual
    - Since Dolly, there have been several other animals cloned
- Attempts at Human Cloning
    - Therapeutic Cloning - production of stem cells used to treat disease; produces stem cells to attempt to remedy detrimental diseases or defects
    - Therapeutic cloning efforts have met with resistance because of bioethical considerations