Mader/*Biology*, 11/e – Chapter Outline

Chapter 13

13.3 Gene Mutations

1. A **gene mutation** is a permanent change in the sequence of bases in DNA; mutations range from having no effect to total inactivity.

A. Causes of Mutations
   1. **Spontaneous mutations** result in abnormalities in normal biological processes.
      a. Mutations due to replication errors are very rare.
      b. DNA polymerase constantly proofreads new DNA against the old, and repairs any irregularities, thereby reducing mistakes to one out of every one billion nucleotide pairs replicated.
   2. **Induced mutations** are changes in the DNA base sequencing from exposure to toxic chemicals or radiation.
      a. **Carcinogens** are mutagens that increase the chances of cancer.
         1) The Ames test is commonly used to determine if a chemical is carcinogenic.
         2) A histidine-requiring strain of bacteria is exposed to a chemical.
         3) If the chemical is mutagenic, the bacteria regain the ability to grow without histidine.
      b. Tobacco smoke contains a number of known carcinogenic chemicals.
      c. X rays and gamma rays are ionizing radiation that creates free radicals, ionized atoms with unpaired electrons.
      d. Ultraviolet (UV) radiation is easily absorbed by pyrimidines in DNA.
         1) Where two thymine molecules are near each other, UV may bond them together as thymine dimers.
         2) Usually dimers are removed from damaged DNA by special enzymes called **DNA repair enzymes.**

B. Effect of Mutations on Protein Activity
   1. **Point mutations** change a single nucleotide and therefore change a single specific codon.
      a. The effect of the point mutation depends on the specific base change in the codon.
      b. Changes to codons that code for the same amino acid have no effect; e.g., UAU to UAC both code for tyrosine.
      c. A change from UAC to UAG (a *stop* codon) results in a shorter protein, and a change from UAC to CAC incorporate histidine instead of tyrosine.
      d. Sickle cell disease results from a single base change in DNA where the beta-chain of hemoglobin contains valine instead of glutamate at one location and the resulting distorted hemoglobin causes red blood cells to clog vessels and die off sooner.
   2. **Frameshift Mutations** occur most often when one or more nucleotides are either inserted or deleted from DNA.
      a. The reading frame depends on the sequence of codons from the starting point: THE CAT ATE THE RAT.
      b. If, for example, C is deleted, the reading frame is shifted: THE ATA TET HER AT.
      c. Frameshift mutations occur when one or more nucleotides are inserted or deleted from DNA.
      d. The result of a frameshift mutation is a new sequence of codons and nonfunctional proteins.
   3. A single nonfunctional protein can cause dramatic effects.
      a. The human transposon *Alu* is responsible for hemophilia when it places a premature stop codon in the gene for clotting factor IX.
      b. PKU results when a person cannot convert phenylalanine to tyrosine; phenylalanine builds up in the system, leading to mental retardation.
      c. A faulty code for an enzyme in the same pathway results in an albino individual.

d. Cystic fibrosis is due to inheriting a faulty code for a chloride transport protein in the plasma membrane.
e. Androgen insensitivity is due to a faulty receptor for male sex hormones; body cells cannot respond to testosterone and the individual develops as a female (even though all of the body cells are XY).

C. Mutations Can Cause Cancer
1. The development of cancer involves a series of various types of mutations.
2. Tumor-suppressor genes normally act as brakes on cell division when it begins to occur abnormally.
3. When proto-oncogenes mutate, they become oncogenes.
4. Tumor-suppressor genes and proto-oncogenes often code for transcription factors or proteins that control transcription factors.
5. *P53*, a major tumor-suppressor gene, is more frequently mutated in human cancers than any other known gene.
   a. The *p53* protein acts as a transcription factor to turn on the expression of genes whose products are cell cycle inhibitors.
   b. The *p53* can also stimulate apoptosis (programmed cell death).
6. Other proto-oncogenes code for *Ras* proteins, which are needed for normal cell growth and DNA synthesis.