**Chapter 7**

**Genetically Modified Organisms  
Gene Expression, Mutation, and Cloning**

**Protein Synthesis and Gene Expression**

* In the early 1980s, genetic engineers began producing recombinant bovine growth hormone (rBGH)
  + Made by genetically engineered bacteria
  + The bacteria were given DNA that carries instructions for making BGH
  + In cows, growth hormones increase body size and milk production

**Protein Synthesis and Gene Expression: From Gene to Protein**

* **Protein synthesis** – the process of using instructions carried on a **gene** to create proteins.
* Several steps are involved and require both **DNA** and **RNA**.
  + **Gene** –a sequence of DNA that encodes a protein
  + **Protein** – a large molecule composed of amino acids
* DNA
  + Double-stranded
  + Each **nucleotide** composed of deoxyribose, phosphate, and nitrogenous base
  + 4 bases: adenine, thymine, guanine, cytosine
* RNA
  + Single-stranded
  + Nucleotides comprised of **ribose**, phosphate, and nitrogenous base
  + 4 bases: A, C, G, and Uracil
* The flow of genetic information in a cell is   
  **DNA** → **RNA** → **protein** and occurs in 2 steps:
  + **Transcription** (DNA → RNA)
  + **Translation** (RNA → Protein)

**Protein Synthesis and Gene Expression: Transcription**

* Transcription occurs in the nucleus.
  + **RNA polymerase** binds to the **promoter** region of the gene.
  + **RNA polymerase** zips down the length of gene, matching RNA nucleotides with complementary DNA nucleotides
  + This forms messenger RNA (mRNA)

**Protein Synthesis and Gene Expression: Translation**

* Translation occurs in the cytoplasm (outside the nucleus).
* Translation requires: mRNA (made during transcription), amino acids, energy (ATP), and   
  some helper molecules.
  + Ribosomes
  + Transfer RNA (tRNA)
* **Ribosomes**
* The ribosome is composed of **ribosomal RNA (rRNA)** and comprises a small and   
  a large subunit.
* **Transfer RNA:** tRNA carries amino acids and matches its **anticodon** with **codons** on mRNA
* Codons are 3 nucleotides long

**Protein Synthesis and Gene Expression: Genetic Code**

* The genetic code allows a specific codon to code   
  for a specific amino acid.
  + A codon is comprised of three nucleotides = 64 possible combinations (43 combinations)
  + 61 codons code for amino acids
  + 3 others are **stop codons**, which end protein synthesis
  + Genetic code expresses *redundancy*
  + The genetic code is *universal*

**Protein Synthesis and Gene Expression: Mutations**

* Changes in genetic sequence = **mutations**
* Changes in genetic sequence *might* affect the order of amino acids in a protein.
  + Protein function is dependent on the precise order of amino acids
  + Possible outcomes of mutation:

1 - no change in protein

2 - non-functional protein

3 - different protein

* **Base-substitution mutation**
  + Simple substitution of one base for another
* **Neutral mutation**
  + Mutation does not change the function of the protein, it codes for the same amino acid
* **Frameshift mutation** 
  + Addition or deletion of a base, which changes the **reading frame**

**Protein Synthesis and Gene Expression: An Overview of Gene Expression**

* Each cell in your body (except sperm and   
  egg cells) has the same DNA.
* But each cell only expresses a small   
  percentage of genes.
  + Example: Nerve and muscle cells perform very different functions, thus they use different genes.
  + Turning a gene or a set of genes on or   
    off = **regulating gene expression**
* Nerves and cells have the same suite of genes, but they **express** different genes.

**Protein Synthesis and Gene Expression: Regulating Gene Expression**

* Regulation of transcription
  + Prokaryotic cells use **repressors** to regulate gene expression
    - Repressors bind to the promoter and prevent the RNA polymerase from binding
* Regulation of transcription
  + Eukaryotic cells use **activators** to regulate gene expression
    - Activators help the RNA polymerase bind to the promoter

**Producing Recombinant Proteins: Cloning a Gene Using Bacteria**

* rBGH is a protein, and is coded by a specific gene.
  + Transfer of rBGH gene to bacteria allows for growth under ideal conditions.
  + Bacteria can serve as “factories” for production of rBGH.
  + **Cloning** of the gene is making many copies of that gene.
* **Restriction enzymes** – Used by bacteria as a form of defense. Restriction enzymes cut DNA at specific sequences. They are important in biotechnology because they allow scientists to make precise cuts in DNA.
* **Plasmid** – Small, circular piece of bacterial DNA that exists separate from the bacterial chromosome. Plasmids are important because they can act as a ferry to carry a gene into a cell.
* Step 1. Remove the gene from the cow chromosome
* Step 2. Insert the BGH gene into the bacterial plasmid
* **Recombinant** – Indicates material that has been genetically engineered: a gene that has been removed from its original genome and combined with another.
* After step 2, the GBH is now referred to as recombinant GBH or **rGBH**.
* Step 3. Insert the recombinant plasmid into a bacterial cell
* About 1/3 of cows in the US are injected with rBGH. rBGH increases milk volume from cows by about 20%.
* The same principles apply to other proteins.
  + Clotting proteins for hemophiliacs are produced using similar methods.
  + Insulin for diabetics is also produced in this way.
* FDA approval is needed for any new food that is not **generally recognized as safe (GRAS).**

**Genetically Modified Foods**

* Unlike rBGH, crop plants are directly modified. In order to do this, the target gene must be inserted into the plant cell. Two methods to do this:
  + **Ti plasmid**
  + **Gene gun**
* **Transgenic organism** – the result of the incorporation of a gene from one organism to the genome of another. Also referred to   
  as a **genetically modified organism (GMO).**
* Benefits: Crops can be engineered for resistance to pests, thus farmers can spray fewer chemicals.
* Concerns: Pests can become resistant to chemicals. GM crops may actually lead to increased use of pesticides and herbicides. GM crop plants may transfer genes to wild relatives.

**Genetically Modified Humans: Stem Cells**

* **Stem cells** – **undifferentiated** cells, capable of growing in to many different kinds of cells and tissues
* Stems cells might be used to treat **degenerative diseases** such as Alzheimer’s or Parkinson’s.
* Using stem cells to produce healthy tissue is called **therapeutic cloning**.
  + Stem cells could also be used to grow specific tissues to treat burns, heart attack damage, or replacement cartilage in joints.
* Stems cells are **totipotent**, meaning they can become any other cell in the body.

**Genetically Modified Humans: Human Genome Project**

* **Human Genome Project** – international effort to   
  map the sequence of the entire human genome (~20,000 – 25,000 genes).
  + For comparative purposes, genomes of other **model organisms** (*E. coli*, yeast, fruit flies, mice) were also mapped.
  + It was sequenced using the technique of *chromosome walking***.-**

**Genetically Modified Humans: Gene Therapy**

* **Gene therapy –** replacement of defective genes with functional genes
  + Germ line gene therapy
    - Embryonic treatment
    - Embryo supplied with a functional version of the defective gene.
    - Embryo + cells produced by cell division have a functional version of gene.
  + **Somatic cell gene therapy**
    - Somatic cell therapy used as a treatment of SCID (severe combined immunodeficiency)
* All somatic cells have limited lifetimes.
* Therapy is not permanent and requires several treatments per year.

**Genetically Modified Humans: Cloning Humans**

* Human cloning occurs naturally whenever identical twins are produced.
  + Cloning of offspring from adults has already been done with cattle, goats, mice, cats, pigs, and sheep.
  + Cloning is achieved through the process of **nuclear transfer**.