**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**.