Chapter 9
Gene Regulation
Part 2
Other topics in Chp 9 Part 2

- Protein folding diseases

- Most diseases are caused by mutations in the DNA that result in changes in all four levels of protein structure (Alzheimer, Huntington, Parkinson diseases)

- A few diseases are caused by proteins that simply change their own $3^\text{O}$ or $4^\text{O}$ structure, their new three-dimensional structure can then cause disease
  - These include prion diseases such as Creutzfeldt-Jakob disease and mad-cow disease
9.8 Regulation of Gene Expression

- Regulation of protein synthesis occurs at several levels:
  - Timing of transcription
  - Alternative splicing of mRNA
  - The rate of translation
  - The rates at which proteins are processed
  - The rate of protein break-down
Transcriptional regulation
- Chromatin remodeling to make genes accessible for transcription
- Regulation of transcription initiation

Determines which genes are translated

Post-transcriptional regulation
- Variations in pre-mRNA processing
- Variations in rate of mRNA breakdown
- RNA interference

Determines types and availability of mRNAs to ribosomes

Translational regulation
- Variations in rate of initiation of protein synthesis

Determines rate at which proteins are made

Post-translational regulation
- Variations in rate of protein processing
- Variations in rate of protein breakdown

Determines availability of finished proteins
9.6 Effects of Protein Processing

- Humans have more than 25,000 protein-coding genes, but can make over 100,000 different proteins.

- Taking into account alternative splicing and protein modification in the Golgi (Chp 2) it is estimated that each gene can make 6 or 7 different proteins.

- **Proteome**
  - The set of proteins made by a particular cell type (Chapter 15)
9.8 Several Mechanisms Regulate the Expression of Genes

*transcription factors* control which genes are expressed
- contain DNA-binding domains
- initiate transcription
- about 2,000 in humans

Mutations in transcription factors may cause a wide range of effects
Histones play major role in gene expression
- Expose DNA when and where it is to be transcribed and shield it when it is to be silenced

The three major types of small molecules that bind to histones are:
- Methyl groups—no transcription $\rightarrow$ OFF
- Acetyl group—allow transcription $\rightarrow$ ON
- Phosphate groups—allow $\rightarrow$ ON
Chemical groups that bind histones

Transcription OFF

- Methyls (CH₃)

Transcription ON

+ acetyl groups (CH₃CO₂)
+ phosphates (PO₄)

The changes to the DNA are known as **epigenetic changes** (outside the gene).

**Failure to remove acetyl groups and failure to add methyl groups are known to cause human disorders including ICF syndrome and Rett syndrome.**
RNA Interference

- MicroRNAs are noncoding RNAs
- They are 21-22 bases long
- The human genome has about 1,000 distinct microRNAs that regulate at least 1/3rd of the protein-encoding genes
- When a microRNA binds to a “target” mRNA, it prevents translation causing it to be degraded
- Synthetic micro RNA molecules can be introduced into selected cells to block gene expression—cancer therapy
Chapter 10
From Proteins to Phenotypes
10.1 Proteins Are the Link Between Genes and the Phenotype

- Proteins are essential components of all biological structures and processes
- Proteins are the end product of gene expression
- Phenotypes are the visible end product of a chain of events that starts with the gene, the mRNA, and the protein product
Mutant Gene Products

- Proteins can act as growth hormones, receptors, and metabolic enzymes
- Mutated genes can produce abnormal or non-functional proteins that produce changes in phenotypes
- Most phenotypes we see today are not new.
Pharmacogenetics

- **Pharmacogenetics**
  - A branch of genetics focused on inheritable differences in the response to drugs

- Variations in the amino acid sequences of proteins affect the way individuals react to prescription drugs and chemicals in the environment
Drug Sensitivities are Genetic Traits

- Succinylcholine sensitivity - Sensitivity to anesthetics
  - Having a form of serum cholinesterase that breaks down the anesthetic very slowly

- Gene variations and breast cancer therapy
  - Estrogen sensitivity is treated with tamoxifen
  - Women with poor tamoxifen metabolism have higher risk of recurrence
Ecogenetics

- The study of genetic variation that affects responses to environmental chemicals

Some individuals may be sensitive or resistant to environmental chemicals such as pesticides
  - Important in research, medicine, and public policy
Ecogenetics

- Sensitivity of people to pesticides such as parathion is genetically controlled by alleles of the gene for the enzyme paraoxonase
Small differences in DNA can lead to differences in proteins that can have a large effect on individual phenotype and one’s ability to taste, smell, and metabolize medicines or other chemicals.