Chapter 10: Gene Expression and Regulation

OVERVIEW

In this chapter you will learn how genes are expressed and regulated. The authors introduce the "one-gene, one-protein" hypothesis. They discuss the processes of transcription, during which information in DNA molecules makes RNA, and translation, during which the information in RNA molecules makes proteins. You also will learn about the three types of RNA and their functions, as well as transcriptional regulation of genes in eukaryotic cells and the effects of mutation.

Boys and girls have many physical differences that are biologically determined. However, the genes of men and women do not differ so dramatically. In fact, boys have all the genes needed to make female genitalia, and girls have all the genes needed to make male genitalia. In boys, the action of a single gene activates the male developmental pathway and deactivates the female pathway. How does this gene work?

1) How Are Genes and Proteins Related?

The information in DNA must be linked to proteins, since proteins are responsible for building cell components and carrying out biochemical reactions. Within a biochemical pathway, the product of one enzyme becomes the substrate of the next enzyme in the pathway. Using mold (Neurospora) with single doses of chromosomes and **genes** in its cells, Beadle and Tatum used X-rays to cause mutations (changes in the base sequence of DNA). Each mutation caused the loss of the ability of Neurospora to make one enzyme. Thus, a mutation in a single gene affected only a single enzyme within a single biochemical pathway. Data supported the hypothesis that each gene encodes information (as sequence of bases) needed for making one specific protein (an amino acid sequence): the "one-gene, one-enzyme" relationship. Most genes contain the information for the synthesis of a single protein. Some genes code for structural proteins or for types of **RNA** (**ribonucleic acid**), but most code for enzymes. Some functional proteins have more than one subunit, each subunit made by a different gene, so the "one-gene, one-enzyme" relationship has been clarified to become the "one-gene, one-**polypeptide**" relationship.

DNA in the nucleus provides instructions for protein synthesis in the cytoplasm via RNA intermediaries. RNA differs from DNA in three ways: RNA is single stranded, RNA has the sugar ribose instead of deoxyribose in its backbone, and RNA has the base uracil instead of thymine. DNA codes for three kinds of RNA: **messenger RNA** (**mRNA**), **ribosomal RNA** (**rRNA**), and **transfer RNA** (**tRNA**).

Overview: Genetic information is transcribed into RNA and translated into protein. During **transcription**, the information in DNA is copied into either mRNA, rRNA, or tRNA. Thus, a gene is a segment of DNA that can be transcribed into RNA. **Translation** is catalyzed by RNA polymerase and occurs in the nucleus. During protein synthesis (translation), tRNA and rRNA, together with proteins, use the nucleotide sequence in mRNA to make a specific amino acid sequence within a protein. The rRNA assembles together with dozens of proteins to form **ribosomes**. Translation is catalyzed by ribosomes and occurs in the cytoplasm.

In cells, the language of nucleotide sequences in DNA and mRNA must be translated into the language of amino acid sequences in proteins. The dictionary for translation is the **genetic code**. In the genetic code, a sequence of three nucleotides specifies an amino acid or a "stop." Four different nucleotide bases must code for 20 different amino acids in protein. A three-base sequence gives 64 possible combinations, more than enough to code for 20 different amino acids. "Words" in the genetic code are three bases long and most signify an amino acid. An RNA with only U bases (UUUUUUUUU...) makes a protein with only phenylalanine (phe-phe-phe...). So, the triplet UUU codes for phenylalanine. The 64 mRNA triplets

are called **codons**. All amino acids begin with the same amino acid methionine, specified by the codon AUG. Three codons, UAG, UAA, and UGA, are **stop codons**, which signal the completion of protein synthesis. Each codon specifies one, and only one, amino acid (except the stop codons).

2) How Is Information in a Gene Transcribed into RNA?

Transcription consists of initiation, elongation, and termination. Initiation of transcription begins when **RNA polymerase** binds to the promoter of a gene. A different version of the enzyme RNA polymerase makes each type of RNA (m, r, and tRNA). RNA polymerase must select the appropriate genes to transcribe in each cell type and at each stage of a cell's life. The enzyme uses a gene's **promoter** region, a non-transcribed sequence of DNA that marks the beginning of the gene. When RNA polymerase binds to the promoter, transcription of that gene begins.

When RNA polymerase binds to the promoter region, it begins to unwind the gene and then travels in one direction along one of the DNA strands, making an RNA molecule that is complementary to that strand of DNA (the template strand). After about 10 nucleotides have been added to the growing RNA chain, the first nucleotides of the RNA molecule separate from the DNA **template strand**, and that region of the gene rewinds. When the RNA polymerase reaches the termination signal, it releases the completed RNA molecule and detaches from the DNA. Transcription is selective, being restricted to only those genes needed by that particular cell type at that particular time. And, transcription copies only the template strand of most genes.

3) How Is the Sequence of a Messenger RNA Molecule Translated into Protein?

Messenger RNA carries the code for the amino acid sequence of a protein from the nucleus into the cytoplasm, while the gene remains safely in the nucleus. Ribosomal RNA forms an important part of the protein-synthesizing machinery of a ribosome. Each ribosome has a large and a small subunit, which remain separate unless the ribosome is making proteins. When active, the small and large ribosomal subunits come together with an mRNA molecule in between them. The large subunit has binding sites for tRNA and a catalytic site for joining the amino acids brought in by the tRNAs.

Transfer RNA molecules decode the sequence of bases in mRNA into the amino acid sequence of a protein. Cells make 61 types of tRNA, one type for each different amino-acid encoding mRNA codon. Each type of tRNA is capable of picking up only one type of amino acid. Each tRNA has three exposed bases, called the **anticodon**, that form base pairs with the mRNA codon. For example, the mRNA codon AUG will attract the tRNA with anticodon UAC carrying the amino acid methionine.

During translation, mRNA, tRNA, and ribosomes cooperate to make proteins. Translation has three steps: initiation (protein synthesis begins when tRNA and mRNA bind to a ribosome), elongation, and termination. In initiation, the first AUG codon in a eukaryotic mRNA sequence specifies where translation will begin. An "initiation complex" (the small ribosomal subunit and a methionine-tRNA) binds to the end of an mRNA and moves along until it encounters the first AUG codon, which base pairs with the UAC anticodon of the methionine tRNA. The large ribosomal subunit then attaches, sandwiching the mRNA between the small and large subunits.

During elongation and termination, protein synthesis proceeds one amino acid at a time until a stop codon is reached. The assembled ribosome holds two mRNA codons in alignment with the two tRNA binding sites in the large subunit. With one tRNA in place, a second tRNA with the complementary anticodon and amino acid moves into the second tRNA binding site on the large subunit, which then breaks the bond holding the first amino acid to its tRNA and forms a peptide bond between the two amino acids. The first tRNA is empty and leaves the ribosome, and the second tRNA has two amino acids bound. The ribosome shifts to the next mRNA codon, moving the second tRNA into the first binding site and allowing the third tRNA to move into place. The third amino acid forms a peptide bond with the second one, which detaches from its tRNA. The empty second tRNA leaves, the ribosome shifts to read the fourth codon, shifting the third tRNA with attached amino acids into the first binding site, and the process continues.

When the ribosome reaches a stop codon, special proteins bind to the ribosome, forcing it to release the finished protein chain and the mRNA, and the ribosome disassembles. A protein 100 amino acids long can be assembled by translation in about 6 seconds.

4) How Do Mutations in DNA Affect the Function of Genes?

Mutations are changes in the sequence of bases in DNA, often through a mistake in base pairing during DNA replication, or triggered by an environmental chemical or radiation. In a **nucleotide substitution** (or **point mutation**), a pair of bases becomes incorrectly matched and the cell replaces the correct base with another incorrect one. An **insertion mutation** occurs when one or more new nucleotide pairs are added into a gene. A **deletion mutation** occurs when one or more nucleotide pairs are removed from a gene. Deletions and insertions can have quite harmful effects on a gene because all the codons that follow the deletion or insertion will be misread.

Mutations have different effects on protein structure and function. Four types of effects may result from mutations: (1) The protein is unchanged. If the gene's base sequence is changed from GAG to GAA (a point mutation), the same amino acid will be incorporated into the protein this gene codes for. (2) The new protein is equivalent to the original one if the active site is unchanged and the rest of the molecule is changed in an insignificant way. This is a **neutral mutation**. For instance, a change from GAG to CAG replaces one hydrophilic amino acid with another. (3) Protein function is changed by an altered amino acid sequence. If GAG changes to GTG, a hydrophilic amino acid is replaced by a hydrophobic one. (4) Protein function is destroyed by a misplaced stop codon, resulting in a much shortened protein chain. If AAG is replaced by TAG, this creates a new stop codon, halting translation prematurely.

Mutations provide the raw material for evolution. Mutation rates vary from 1 in 100,000 to 1 in 1,000,000 gametes. So, a human male releases about 600 mutant sperm during each ejaculation of 300–400 million sperm. If mutations in gametes are not lethal, they may be passed on to future generations. Mutation is the source for genetic variation and thus is essential for evolution.

5) How Are Genes Regulated?

How do cells control the presence, concentration, and activity of the proteins encoded by genes? Proper regulation of gene expression is critical for an organism's development and health. Most cells in the body have identical DNA (30,000 to 50,000 genes) but they don't use all the DNA all the time. Gene expression changes over time, and an organism's environment can determine which genes are translated. Four of the steps at which the rate of gene activity may be regulated are: (1) transcription of individual genes; (2) translation of various mRNAs; (3) modification of inactive proteins into their active forms; and (4) regulation of a protein's lifespan.

Eukaryotic cells may regulate the transcription of (1) individual genes, through the action of regulatory proteins such as steroid hormones; (2) regions of chromosomes with several genes, by condensing those regions into compact DNA that is inaccessible to RNA polymerase; or (3) entire chromosomes with thousands of genes, such as one of the X chromosomes in mammalian females to form a **Barr Body**. Which X chromosome is inactivated in any cell is random, but all its daughter cells will have the same condensed chromosome. For example, separate patches of orange and black fur in female calico cats are due to fur-color genes on the X chromosome.

Case study revisited: boy or girl? The Y chromosome of mammals contains the SRY (sex-determining region on the Y) gene. An XX mouse embryo given the SRY gene develops into a sterile male, indicating that an XX female has all the genes to be a male. Likewise, an XY mouse embryo lacking the SRY gene develops into a female, indicating that an XY male has all the genes to be a female. The SRY gene normally is transcribed for only a short time in embryonic development and only in the cells that will become the testes. The SRY protein initiates the expression of many other genes, the proteins from which are needed for testes development. The testes secrete testosterone, which activates other genes leading to development of the penis and scrotum. So, the SRY gene is the initial genetic switch to activate male development.

KEY TERMS AND CONCEPTS

Fill-In: From the following list of key terms, fill in the blanks in the following statements.

anticodon	messenger RNA	RNA polymerase
codon	mutation	stop codons
deletion mutation	one-gene, one-protein hypothesis	transcription
genetic code	point mutation	transfer RNA
insertion mutations	ribosome	translation

1. The _____ is the amino acid translation of all the codons, each of which directs the incorporation of an amino acid during protein synthesis.

2. The enzyme that catalyzes the covalent bonding of free RNA nucleotides into a continuous strand, using the sequence of bases in DNA as a template, is called _____.

3. The hypothesis that each gene encodes information (as a sequence of bases) needed for making one specific protein (amino acid sequence) is the _____.

4. An _____ is a sequence of three nucleotides in transfer RNA that is complementary to the three nucleotides in messenger RNA.

5. The process in which a sequence of nucleotide bases in mRNA is converted into a sequence of amino acids in a protein is called _____.

6. The mRNA "start codon" is AUG, coding for the first amino acid in a protein. Three codons (UAG, UAA, UGA) are mRNA _____, signaling that the protein's amino acid sequence is completed.

7. A molecule of _____ is a strand of nucleotides, complementary to the DNA of a gene, that conveys genetic information to ribosomes to be used to sequence amino acids during protein synthesis.

8. _____ is the synthesis of an RNA molecule from a DNA template.

9. A change in the base sequence of DNA is called a _____.

10. A molecule that binds to a specific amino acid and has a set of three nucleotides complementary to the codon for that amino acid is known as _____.

11. In a _____, a pair of bases becomes incorrectly matched; _____ occur when one or more new nucleotide pairs are added into a gene; and a _____ occurs when one or more nucleotide pairs are removed from a gene.

12. A _____ is a sequence of three nucleotides of mRNA that specifies a particular amino acid to be incorporated into a protein.

13. An organelle with two subunits, each composed of RNA and protein, that serves as the site of protein synthesis is a _____.

Key Terms and Definitions

androgen insensitivity: a rare condition in which an individual with XY chromosomes is female in appearance because the body's cells don't respond to the male hormones that are present.

anticodon: a sequence of three bases in transfer RNA that is complementary to the three bases of a codon of messenger RNA.

Barr body: an inactivated X chromosome in cells of female mammals, which have two X chromosomes; normally appears as a dark spot in the nucleus.

codon: a sequence of three bases of messenger RNA that specifies a particular amino acid to be incorporated into a protein; certain codons also signal the beginning or end of protein synthesis.

deletion mutation: a mutation in which one or more pairs of nucleotides are removed from a gene.

exon: a segment of DNA in a eukaryotic gene that codes for amino acids in a protein (see also *intron*).

gene: a unit of heredity that encodes the information needed to specify the amino acid sequence of proteins and hence particular traits; a functional segment of DNA located at a particular place on a chromosome.

genetic code: the collection of codons of mRNA, each of which directs the incorporation of a particular amino acid into a protein during protein synthesis.

insertion mutation: a mutation in which one or more pairs of nucleotides are inserted into a gene.

intron: a segment of DNA in a eukaryotic gene that does not code for amino acids in a protein.

messenger RNA (mRNA): a strand of RNA, complementary to the DNA of a gene, that conveys the genetic information in DNA to the ribosomes to be used during protein synthesis; sequences of three bases (codons) in mRNA specify particular amino acids to be incorporated into a protein.

mutation: a change in the base sequence of DNA in a gene; normally refers to a genetic change significant enough to alter the appearance or function of the organism.

neutral mutation: a mutation that has little or no effect on the function of the encoded protein.

nucleotide substitution: a mutation that replaces one nucleotide in a DNA molecule with another; for example, a change from an adenine to a guanine.

point mutation: a mutation in which a single base pair in DNA has been changed.

polypeptide: a short polymer of amino acids; often used as a synonym for protein.

promoter: a specific sequence of DNA to which RNA polymerase binds, initiating gene transcription.

ribonucleic acid (rī-bō-noo-klā´-ik; RNA): a molecule composed of ribose nucleotides, each of which consists of a phosphate group, the sugar ribose, and one of the bases adenine, cytosine, guanine, or uracil; transfers hereditary instructions from the nucleus to the cytoplasm; also the genetic material of some viruses.

ribosomal RNA (rRNA): a type of RNA that combines with proteins to form ribosomes.

ribosome: an organelle consisting of two subunits, each composed of ribosomal RNA and protein; the site of protein synthesis, during which the sequence of bases of messenger RNA is translated into the sequence of amino acids in a protein.

RNA polymerase: in RNA synthesis, an enzyme that catalyzes the bonding of free RNA nucleotides into a continuous strand, using RNA nucleotides that are complementary to those of a strand of DNA.

stop codon: a codon in messenger RNA that stops protein synthesis and causes the completed protein chain to be released from the ribosome.

template strand: the strand of the DNA double helix from which RNA is transcribed.

transcription: the synthesis of an RNA molecule from a DNA template.

transfer RNA (tRNA): a type of RNA that binds to a specific amino acid by means of a set of three bases (the anticodon) on the tRNA that are complementary to the mRNA codon for that amino acid; carries its amino acid to a ribosome during protein synthesis, recognizes a codon of mRNA, and positions its amino acid for incorporation into the growing protein chain.

translation: the process whereby the sequence of bases of messenger RNA is converted into the sequence of amino acids of a protein.

uracil: a nitrogenous base found in RNA; abbreviated as *U*.

Werner syndrome: a rare condition in which a defective gene causes premature aging; caused by a mutation in the gene that codes for DNA replication/repair enzymes.

THINKING THROUGH THE CONCEPTS

True or False: Determine if the statement given is true or false. If it is false, change the underlined word(s) so that the statement reads true.

14. _____ Genes are made of RNA in human cells.
15. _____ Transfer RNA carries amino acids to the ribosomes.
16. _____ Protein synthesis occurs in the ribosome.
17. _____ Messenger RNA is double stranded.
18. _____ Messenger RNA is manufactured in the cytoplasm.
19. _____ The triplets of bases in messenger RNA are called anticodons.
20. _____ Proteins are made during transcription.
21. _____ Proteins contain many nucleotide subunits.
22. _____ Barr bodies are found in normal mammalian females.
23. _____ Barr bodies are active X chromosomes found in mammals.

Identify: Determine whether the following statements refer to **mRNA**, **tRNA**, or **rRNA**.

24. _____ has anticodons
25. _____ deciphers the genetic code
26. _____ carries the genetic code to make proteins
27. _____ picks up and transports amino acids
28. _____ part of ribosomes
29. _____ has codons
30. _____ twisted into a cloverleaf shape
31. _____ fits into binding sites in ribosomes

Identify: Determine whether the following statements refer to **transcription** or **translation**.

32. _____ information from DNA makes RNA
33. _____ information from RNA makes protein
34. _____ occurs in the nucleus of eukaryotic cells
35. _____ occurs in the cytoplasm of eukaryotic cells
36. _____ involves RNA polymerase
37. _____ involves amino acids
38. _____ involves ribosomes
39. _____ involves codon-anticodon interactions
40. _____ involves copying the genetic code
41. _____ involves deciphering the genetic code

Multiple Choice: Pick the most correct choice for each question.

42. Inherited disorders induced by X-rays in red bread mold by Beadle and Tatum
    a. are caused by errors in mitosis
    b. are related to enzyme deficiencies
    c. can always be cured by dietary restrictions
    d. are environmental and not genetic in origin
    e. can never be cured by supplying the missing end product

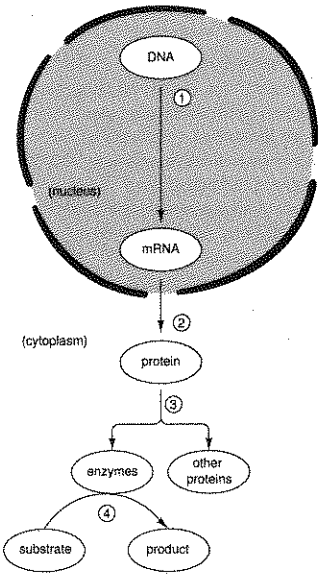
43. If a bacterial protein has 30 amino acids, how many nucleotides are needed to code for it?
    a. 30
    b. 60
    c. 90
    d. 120
    e. 600

44. Which of these choices is coded for by the shortest piece of DNA?
    a. a tRNA having 75 nucleotides
    b. an mRNA having 50 codons
    c. a protein having 40 amino acids
    d. a protein with 2 polypeptides, each having 35 amino acids
    e. an mRNA having 100 bases

45. Blood cells and muscle cells make different enzymes because
    a. blood cells contain only genes for blood cell proteins and muscle cells contain only muscle protein genes
    b. all cells of an organism have all genes
    c. not every gene acts in every type of cell
    d. blood cells have hemoglobin while muscle cells have microtubules
    e. adult red blood cells lack nuclei in mammals

46. Because of random X chromosome inactivation, one of the X chromosomes of a mammalian female
    a. is functionally inactive
    b. is present in each cell in three doses
    c. does not divide during meiosis
    d. disappears from each cell early during development
    e. is genetically identical to the other X chromosome

Fill-In: Based on the figure to the right, answer the following questions.



47. The step indicated by (1) in the figure is commonly known as

    _____.

48. The step indicated by (2) in the figure is commonly known as

    _____.

49. The step indicated by (3) in the figure is commonly known as

    _____.

50. The step indicated by (4) in the figure is commonly known as

    _____.

Fill-In: Fill in the blanks in the following table.

51.

Type of molecule	Sequences of bases or amino acids See text Table 10-3 for genetic code.
DNA template strand	_____ TAG _____ AGC _____ TCA
DNA non-template strand	GAA _____ TTA _____ CCG _____
messenger RNA codons	_____ _____ _____ _____ _____ _____
transfer RNA anticodons	_____ _____ _____ _____ _____ _____
protein amino acid sequence	_____ _____ _____ _____ _____ _____

APPLYING THE CONCEPTS

These practice questions are intended to sharpen your ability to apply critical thinking and analysis to biological concepts covered in this chapter.

Short Answer.

Suppose a section of DNA from a normal gene has the following sequences of bases in one of its polynucleotide strands:

normal base sequence: TACTTTACGTCGTGAAAACGGTAT

If this strand is used to make an mRNA molecule:

52. the base sequence in the mRNA is _____

53. the normal amino acid sequence in the polypeptide is (use text Table 10-3)

_____

Now, suppose a point mutation occurs and a single base (C*) is added (an insertion mutation) to the gene sequence, causing a new altered sequence to occur:

mutant base sequence: TACC*TTTACGTCGTGAAAACGGTAT

If this mutant strand is used to make an mRNA molecule:

54. the base sequence in the mRNA is _____

55. the abnormal amino acid sequence in the polypeptide is (use text Table 10-3)

_____

56. Briefly explain why, in questions 52–55, the addition of a single base in the DNA caused so many amino acids to change in the polypeptide.

_____

_____

_____

57. What sort of evidence exists to back up the claim that mammalian females have all the genes to develop into a male?

_____

_____

_____

_____

_____

58. What sort of evidence exists to back up the claim that mammalian males have all the genes to develop into a female?

_____

_____

_____

_____

59. Are male calico cats expected in a normal cat population? How could they occur?

Use the Case Study and the Web sites for this chapter to answer the following questions.

60. The SRY region of the Y chromosome has been shown to code for a factor that is "necessary and sufficient" for male physiological development. What is the experimental evidence for the essential role of SRY?

61. Are individuals with XXY (Klinefelter syndrome) male or female? How about individuals with Turner syndrome (XO), XYY individuals, or XXX individuals? Are they capable of reproducing?

62. What biological errors of metabolism result in XY females? Consider gene rearrangements and the SRY gene. How could an XX individual be physiologically male?