Molecular Biology of the Gene 10

Most biologists would agree that the most significant biological discovery of the twentieth century was the discovery of the structure of the gene. At the beginning of the century Mendel's rules were rediscovered, and genes were traced to the chromosomes. Soon it was possible to map the locations of genes, and scientists started wondering what exactly genes were made of and how they shaped an organism. By mid-century, it was clear that DNA is the genetic material and that genes act by directing the synthesis of proteins. Soon researchers discovered the double helix structure of DNA and deciphered the genetic code by which DNA shapes the body. Then scientists learned how to make genes and move them from one organism to another. As the twenty-first century begins, biologists map entire genomes and use their knowledge of genetics to reshape organisms, fight disease, and trace evolution. This chapter describes the molecular biology of the gene and the discoveries that continue to enlarge our understanding of genes.

Organizing Your Knowledge

Exercise 1 (Modules 10.1 - 10.3)

Web/CD Activity 10A *The Hershey-Chase Experiment*
Web/CD Activity 10B *Phage T2 Reproductive Cycle*
Web/CD Activity 10C *DNA and RNA Structure*
Web/CD Activity 10D *The DNA Double Helix*

Review the discovery that DNA is the genetic material, and the structures of DNA and RNA. Then match each phrase on the right with the correct term(s) on the left. Note that some answers are used more than once, and some questions have multiple answers.

A. Adenine (A)
B. Base
C. Cytosine (C)
D. DNA
E. *E. coli*
F. Double helix
G. Guanine (G)
H. Hydrogen bond
I. Radioactive isotope
J. Covalent bond
K. Bacteriophage
L. Protein
M. Nucleic acid
N. Nucleotide
O. Centrifuge
P. Phosphate
Q. Polynucleotide
R. RNA
S. Sugar
T. Thymine (T)
U. Uracil (U)

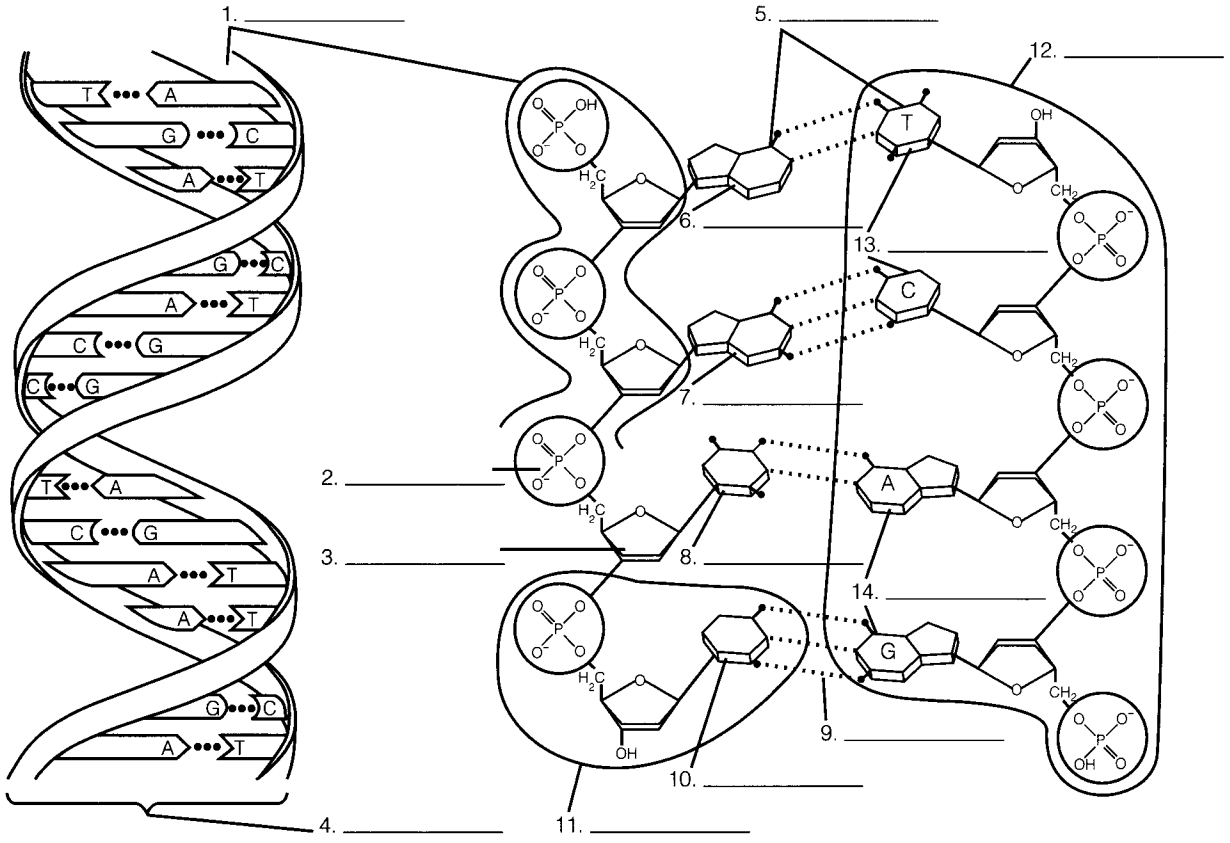
_____ 1. The basic chemical unit of a nucleic acid
_____ 2. The "transforming factor" that alters pneumonia bacteria
_____ 3. The two kinds of nucleic acids
_____ 4. The three parts of every nucleotide
_____ 5. A pair of these forms a "rung" in the DNA ladder
_____ 6. Used to "label" DNA and protein in experiments
_____ 7. The component of a bacteriophage that enters the host cell
_____ 8. Two alternating parts that form the nucleic acid "backbone"
_____ 9. The four bases in DNA
_____ 10. The DNA base complementary to T
_____ 11. A virus that attacks bacteria
_____ 12. The substance a phage leaves outside its host cell
_____ 13. Ribose in RNA and deoxyribose in DNA
_____ 14. Watson and Crick deduced the structure of this molecule
_____ 15. The four bases in RNA
_____ 16. The DNA base complementary to G
_____ 17. A bacterium attacked by T2 and T4 phages
_____ 18. The sequence of these encodes DNA information
_____ 19. Eukaryotic chromosomes consist of this and DNA
_____ 20. The overall shape of a DNA molecule

_____ 21. Links adjacent nucleotides in a polynucleotide chain
_____ 22. Machine used to separate particles of different weights
_____ 23. Links a complementary pair of bases together
_____ 24. A polymer of nucleotides
_____ 25. RNA base that is not in DNA

Exercise 2 (Modules 10.2 – 10.3)

Web/CD Activity 10C *DNA and RNA Structure*
Web/CD Activity 10D *The DNA Double Helix*

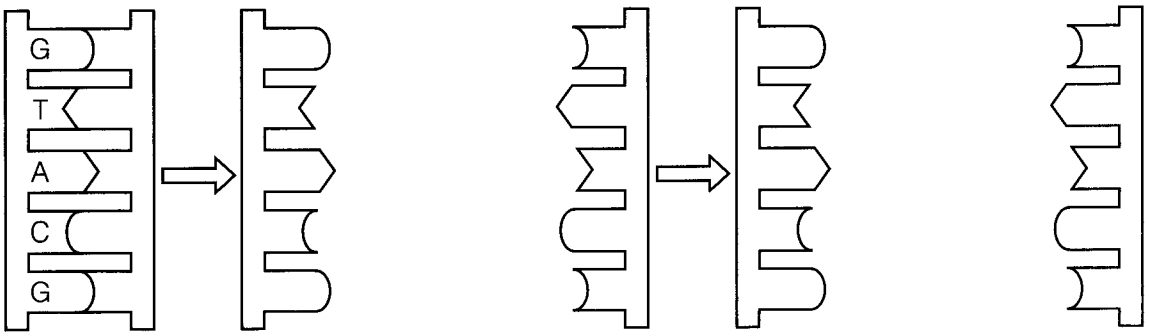
Review the structure of DNA by labeling these diagrams. Include **nucleotide, polynucleotide, sugar (deoxyribose), phosphate group, sugar-phosphate backbone, pyrimidine bases, purine bases, thymine (T), adenine (A), guanine (G), cytosine (C), hydrogen bond, complementary base pair,** and **double helix.**



Exercise 3 (Module 10.4)

Web/CD Activity 10E *DNA Replication: An Overview*

Reproduction and inheritance involve copying DNA instructions, so that they can be passed to the next generation. This process is carried out by DNA polymerases, enzymes that use each strand of the DNA helix as a template on which to build a complementary strand. Review DNA replication by completing the simplified diagrams below. The first diagram shows the parent DNA molecule; label the nucleotides in the right-hand strand. Complete and label the second diagram, so that it shows the parent strands separating and being used as templates. Label the third diagram, so that it shows two completed daughter molecules of DNA. Color the original DNA strands blue and the new strands red.

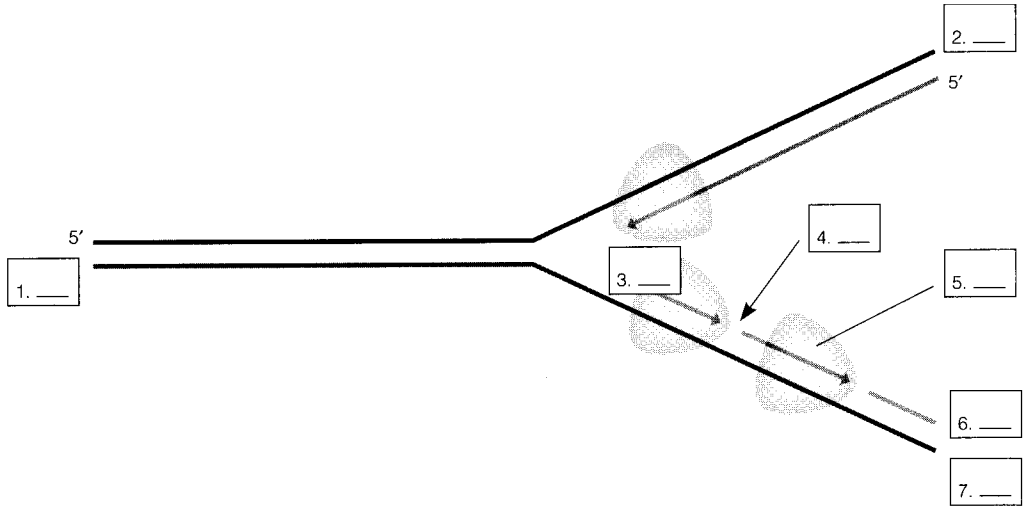


Exercise 4 (Module 10.5)

Web/CD Activity 10F *DNA Replication: A Closer Look*

This module describes some of the ins and outs of DNA replication. Look at the diagrams carefully. Then see if you can match each of the numbers in the boxes on the diagram below with one of the lettered choices. Choices may be used more than once.

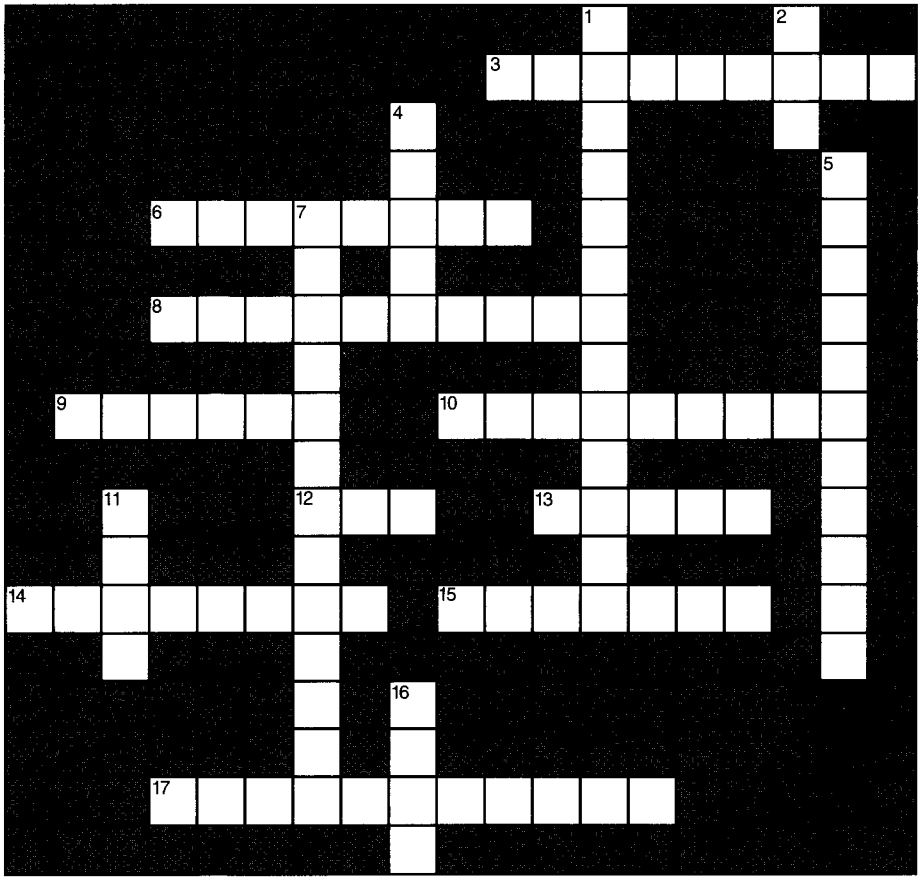
A. 5′ end of daughter strand
B. 3′ end of daughter strand
C. 5′ end of parental strand
D. 3′ end of parental strand
E. DNA polymerase
F. where DNA ligase will unite pieces



Exercise 5 (Modules 10.6 - 10.7)

Web/CD Activity 10G *Overview of the Protein Synthesis*

In a cell, the genotype—genetic information in DNA—is expressed as phenotype in the form of proteins—structural proteins that shape the organism and enzymes that carry out metabolism. Review the relationship between genotype and phenotype by completing this crossword puzzle.



Across

3. A gene consists of hundreds or ____ of nucleotide bases.
6. The information in DNA specifies the synthesis of ____.
8. Garrod noted the gene-protein link in "inborn errors of ____."
9. Genetic instructions are written in 3-base "words" called ____.
10. An organism's expressed traits (what it looks like) make up its ____.
12. To make a protein, DNA information is first transcribed into ____.
13. The DNA language consists of a linear sequence of nucleotide ____.
14. The ____ is an organism's genetic makeup.
15. Phenotype is expressed via structural proteins and ____.
17. Making a polypeptide according to an RNA message is called ____.

Down

1. The base sequence of RNA is ____ to the DNA from which it is transcribed.
2. Genotype is the inheritable information encoded in ____.
4. Each codon in DNA and RNA specifies a certain ____ acid in a polypeptide.
5. Translation is conversion of an RNA message into a ____.
7. Transfer of information from DNA into an RNA molecule is called ____.
11. One ____ specifies how to build one polypeptide.
16. Using bread ____, Beadle and Tatum showed that a gene codes for an enzyme.

Exercise 6 (Modules 10.7 - 10.14)

Web/CD Activity 10H *Transcription*
Web/CD Activity 10I *Translation*

These modules explain how the information in a gene is used to build a protein. Review the processes of transcription and translation by filling in the blanks below.

The first step in making a protein is transcription of a gene. This occurs in the [1]_____ of a eukaryotic cell. An enzyme called [2]_____ carries out the process of transcribing RNA from the DNA. It starts at a specific nucleotide sequence called a [3]_____, next to the gene. RNA polymerase attaches, and the two DNA strands separate. RNA polymerase moves along one strand, and as it does, RNA [4]_____ take their places one at a time along the DNA template. They hydrogen-bond with complementary bases, following the same pairing rules as in DNA—C with G, and U (replacing T in RNA) with A. As the RNA molecule elongates, it peels away from the DNA. Finally, the enzyme reaches the [5]_____, a base sequence that signals the end of the gene, and the polymerase molecule lets go of the gene and the RNA molecule. In a prokaryote, the RNA transcribed from a gene, called [6]_____ (mRNA), can be used immediately in polypeptide synthesis. In a eukaryotic cell, the RNA is further modified, or [7]_____, before leaving the nucleus as mRNA. Extra nucleotides are added to the ends of the transcript, and noncoding regions called [8]_____ are removed. The remaining [9]_____ are spliced together to from a continuous coding sequence. The finished mRNA leaves the nucleus and enters the [10]_____, where translation takes place.

Translation of the "words" of the mRNA message into the [11]_____ sequence of a protein requires an interpreter—[12]_____ (tRNA)—which links the appropriate [13]_____ with each [14]_____ in the mRNA message. A tRNA molecule is a folded strand of RNA. At one end, a special [15]_____ attaches a specific amino acid. The other end of the tRNA molecule bears three bases called the [16]_____, which is complementary to a particular mRNA codon. During the translation process, the tRNA matches its amino acid with an mRNA codon.

[17]_____ are the "factories" where the information in mRNA is translated and polypeptide chains are constructed. A ribosome consists of protein and [18]_____(rRNA). Each ribosome has a groove that serves as a binding site for mRNA. There are two binding sites for tRNA: The P site holds the tRNA carrying the growing [19]_____, while the A site holds a tRNA bearing the next amino acid.

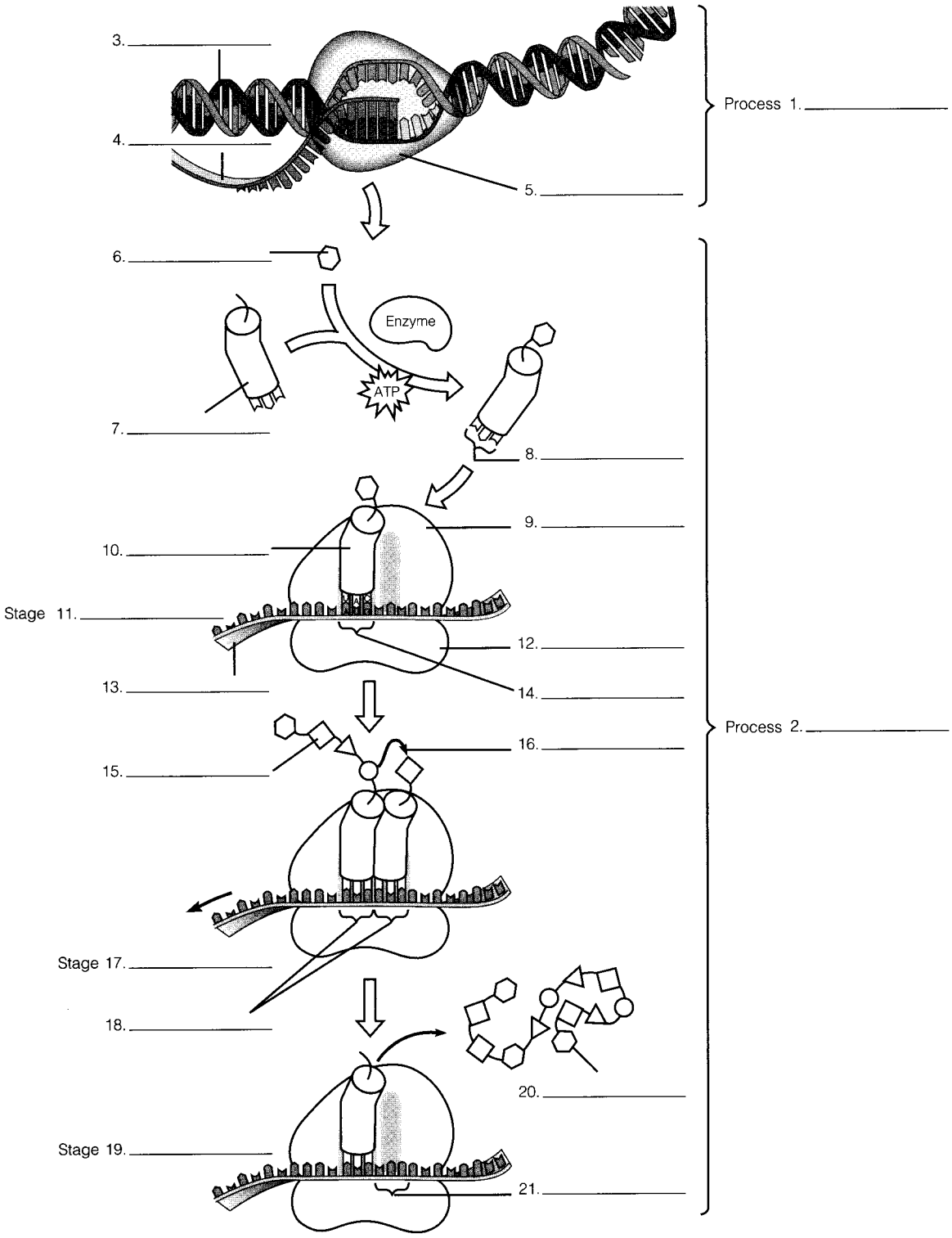
Translation begins with initiation. An mRNA and a special [20]_____ tRNA bind to the ribosome and a specific mRNA codon, the [21]_____, where translation begins. The initiator tRNA generally carries the amino acid methionine (Met). Its anticodon UAC binds to the start codon, AUG. The initiator tRNA fits into the P site on the ribosome.

The next step in [22]_____synthesis is elongation—adding amino acids to the growing chain. The anticodon of an incoming tRNA, carrying its amino acid, pairs with the mRNA codon at the open A site. With help from the ribosome, the polypeptide separates from its tRNA and forms a peptide bond with the [23]_____ attached to the tRNA in the A site. Then the "empty" tRNA in the P site leaves the ribosome, and the tRNA in the A site, with the polypeptide chain, is shifted to the P site. The mRNA and tRNA move as a unit, allowing the next codon to enter the A site. Another tRNA, with a complementary anticodon, brings its amino acid to the A site. Its amino acid is added to the chain, the tRNA leaves, and the complex shifts again. In this way, [24]_____ are added to the chain, one at a time.

Finally, a [25]_____ reaches the A site of the [26]_____, terminating the polypeptide. A stop codon causes the polypeptide to separate from the last tRNA and the [27]_____. The polypeptide folds up, and it may join with other polypeptides to form a larger [28]_____ molecule.

Exercise 7 (Module 10.15)

This module summarizes the key steps in the flow of genetic information from DNA to protein. Study the diagrams carefully, then label the numbered parts and processes.



Exercise 8 (Modules 10.8 and 10.16)

These modules describe the genetic code, how biologists cracked the code, and how mutations change the meaning of the coded genetic message. Use the genetic code chart (Figure 10.8A in the textbook) to translate the following mRNAs into amino acid sequences and answer the questions.

mRNA nucleotide sequence:
(mRNA 1)

1. Amino acid sequence:

Mutation in mRNA:
(mRNA 2)

2. Amino acid sequence:
3. Number of bases changed in mRNA:
4. Type of mutation:
5. Number of amino acids changed:

Mutation in mRNA:
(mRNA 3; compare to 1)

6. Amino acid sequence:
7. Number of bases changed in mRNA (look carefully!):
8. Type of mutation:
9. Number of amino acids changed (compared to mRNA 1):
10. Which mutation had the greatest effect and why?

Exercise 9 (Modules 10.17 – 10.22)

Web/CD Activity 10J *Phage Lysogenic and Lytic Cycles*
Web/CD Activity 10K *Simplified Reproductive Cycle of a DNA Virus*
Web/CD Activity 10L *Retrovirus (HIV) Reproductive Cycle*

These modules describe the structures and life cycles of viruses. Match each phrase on the right with a term from the left. Some answers are used more than once.

A. RNA viruses
B. Prophage
C. AIDS
D. Glycoprotein spikes
E. Virus
F. DNA
G. Lytic cycle
H. Vaccine
I. Nucleus
J. Membranous envelope
K. Bacteriophage
L. Provirus
M. HIV
N. Reverse transcriptase
O. Lysogenic cycle
P. Retrovirus
Q. White blood cell
R. Prophage genes
S. Tobacco mosaic
T. Plasma membrane
U. RNA
V. Cytoplasm
W. Hantavirus
X. Ebola virus

____ 1. Consists of nucleic acid packaged in protein
____ 2. Leads quickly to breaking open of host cell
____ 3. Phage DNA inserted into bacterial chromosome
____ 4. When virus "hides" as part of bacterial chromosome
____ 5. Responsible for toxins of diphtheria, botulism
____ 6. Rod-shaped plant virus
____ 7. This or DNA may be virus genetic material
____ 8. Cause of flu, colds, polio, mumps, AIDS
____ 9. Helps flu or mumps virus enter and leave host cell
____ 10. Used by mumps virus or HIV to attach to host receptors
____ 11. Mumps virus reproduces here
____ 12. Mumps virus makes this and protein from RNA template
____ 13. Mumps virus gets envelope from this part of host cell
____ 14. Herpesvirus reproduces here
____ 15. Genetic material of herpesvirus
____ 16. DNA of herpesvirus inserted into host cell DNA
____ 17. Can be used to prevent a viral disease
____ 18. Virus that causes AIDS
____ 19. Genetic material of HIV
____ 20. RNA virus that reproduces by means of DNA
____ 21. Enzyme that can make DNA from RNA template
____ 22. Form in which HIV "hides" in host cell
____ 23. Acquired immune deficiency syndrome
____ 24. Kind of cell infected by HIV
____ 25. Causes an African hemorrhagic fever
____ 26. Virus like T2 that infects bacteria
____ 27. An RNA virus carried by rodents

Testing Your Knowledge

Multiple Choice

1. In an important experiment, bacteriophages were allowed to infect bacteria. In the first trial, the phages used contained radioactive DNA, and radioactivity was detected in the bacteria. Next, other phages containing radioactive protein were allowed to infect bacteria, and no radioactivity was detected in the bacteria. When the experimenters compared the results of these two trials, they concluded that
   a. genes are made of DNA.
   b. bacteriophages can infect bacteria.
   c. DNA is made of nucleotides.
   d. genes carry information for making proteins.
   e. genes are on chromosomes.

2. An RNA or DNA molecule is a polymer made of subunits called
   a. bases.
   b. amino acids.
   c. nucleotides.
   d. nucleic acids.
   e. pyrimidines.

3. The information carried by a DNA molecule is in
   a. its amino acid sequence.
   b. the sugars and phosphates forming its backbone.
   c. the order of the bases in the molecule.
   d. the total number of nucleotides it contains.
   e. the RNA units that make up the molecule.

4. A gene is
   a. the same thing as a chromosome.
   b. the information for making a polypeptide.
   c. made of RNA.
   d. made by a ribosome.
   e. made of protein.

5. DNA replication occurs
   a. whenever a cell makes protein.
   b. to repair gene damage caused by mutation.
   c. before a cell divides.
   d. whenever a cell needs RNA.
   e. in the cytoplasm of a eukaryotic cell.

6. The flow of information in a cell proceeds
   a. from RNA to DNA to protein.
   b. from protein to RNA to DNA.
   c. from DNA to protein to RNA.
   d. from RNA to protein to DNA.
   e. from DNA to RNA to protein.

7. Which of the following is *not* needed for DNA replication?
   a. ribosomes
   b. DNA
   c. nucleotides
   d. enzymes
   e. All of the above are needed.

8. Which of the following processes occur(s) in the cytoplasm of a eukaryotic cell?
   a. DNA replication
   b. translation
   c. transcription
   d. DNA replication and translation
   e. translation and transcription

9. Beadle and Tatum showed that each kind of mutant bread mold lacked a specific enzyme. This experiment demonstrated that
   a. genes carry information for making proteins.
   b. mutations are changes in genetic information.
   c. genes are made of DNA.
   d. enzymes are required to repair damaged DNA information.
   e. cells need specific enzymes in order to function.

10. During the process of translation (polypeptide synthesis), ____ matches a nucleic acid codon with the proper amino acid.
    a. a ribosome
    b. DNA polymerase
    c. ATP
    d. transfer RNA
    e. messenger RNA

11. How does RNA polymerase "know" where to start transcribing a gene into mRNA?
    a. It starts at one end of the chromosome.
    b. Transfer RNA acts to translate the message to RNA polymerase.
    c. It starts at a certain nucleotide sequence called a promoter.
    d. The ribosome directs it to the correct portion of the DNA molecule.
    e. It looks for the AUG start codon.

12. When RNA is being made, the RNA base ___ always pairs with the base ___ in DNA.
    a. U . . . T
    b. T . . . G
    c. U . . . A
    d. A . . . U
    e. T . . . A

13. A mutagen is
    a. a gene that has been altered by a mutation.
    b. something that causes a mutation.
    c. an organism that has been changed by a mutation.
    d. the portion of a chromosome altered by a mutation.
    e. any change in the nucleotide sequence of DNA.
14. How do retroviruses, such as HIV, differ from other viruses?
    a. They are much simpler than other viruses.
    b. They contain DNA that is used as a template to make RNA.
    c. They can reproduce only inside of living cells.
    d. They contain nucleic acids that code for the making of proteins.
    e. They contain RNA that is used as a template to make DNA.

Essay

1. Sketch a short piece of a DNA molecule, five base pairs long. Use simple shapes to represent bases, sugars, and phosphates. Show proper base pairing, and label a nucleotide, a base, a phosphate group, a sugar, A, C, T, G, the double helix, and hydrogen bonds.
2. Explain why, in DNA, T pairs only with A and not with C or G.
3. Why does it take a group of three DNA nucleotides to specify one amino acid in a protein? Wouldn't it be simpler to have a one-to-one code, where one nucleotide specified one amino acid?
4. What is a mutation? What causes mutations? Why are most mutations harmful? Why aren't all mutations harmful?
5. Which type of mutation—a base substitution or a base deletion—is likely to have the greatest effect on the organism? Why?
6. Describe step by step, but in simple terms, the roles of mRNA, tRNA, ribosomes, and amino acids in making a polypeptide.

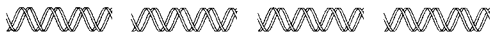
Applying Your Knowledge

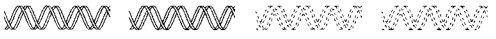
Multiple Choice

1. Which of the following are arranged in the correct order by size, from largest to smallest?
    a. chromosome-gene-codon-nucleotide
    b. nucleotide-chromosome-gene-codon
    c. codon-chromosome-gene-nucleotide
    d. gene-chromosome-codon-nucleotide
    e. chromosome-gene-nucleotide-codon
2. A geneticist raised a crop of T2 bacteriophages in a medium containing radioactive phosphorus, so that the DNA of the bacteriophages was labeled with radioactivity. The labeled phages were then allowed to infect nonradioactive bacteria. In a few hours, these bacteria burst open, releasing many bacteriophages. Some of these phages contained labeled
    a. DNA.
    b. RNA.
    c. protein.
    d. all of the above.
    e. DNA and protein only.
3. A messenger RNA molecule for making a protein is made in the nucleus and sent out to a ribosome. The ribosome reads the mRNA message and makes a protein containing 120 amino acids. The mRNA consisted of at least how many codons?
    a. 30
    b. 40
    c. 120
    d. 360
    e. 480
4. The nucleotide sequence of a DNA codon is ACT. A messenger RNA molecule with a complementary codon is transcribed from the DNA. In the process of protein synthesis, a transfer RNA pairs with the mRNA codon. What is the nucleotide sequence of the tRNA anticodon? (Careful—this one is harder than it appears.)
    a. TGA
    b. UGA
    c. ACT
    d. TGU
    e. ACU

5. Imagine an error occurring during DNA replication in a cell, so that where there is supposed to be a T in one of the genes there is instead a G. What effect will this probably have on the cell?
   a. Each of its kinds of proteins will contain an incorrect amino acid.
   b. An amino acid will be missing from each of its kinds of proteins.
   c. One of its kinds of proteins might contain an incorrect amino acid.
   d. An amino acid will be missing from one of its kinds of proteins.
   e. The amino acid sequence of one of its kinds of proteins will be completely changed.

6. A cell is grown in a solution containing radioactive nucleotides, so that its DNA is labeled with radioactivity. It is removed from the radioactive solution and grown in a normal medium, so that any new DNA strands it makes will not be radioactive. In the normal medium, the cell replicates its DNA and divides. The two daughter cells also replicate their DNA and divide, producing a total of four cells. If a dotted line represents a radioactive DNA strand and a solid line represents a nonradioactive DNA strand, which of the following depicts the DNA of the four cells?

   a. 

   b. 

   c. 

   d. 

   e. 

7. A particular ____ carry the information for making a particular polypeptide, but ____ can be used to make any polypeptide.
   a. gene and ribosome . . . a tRNA and an mRNA
   b. gene and mRNA . . . a ribosome and a tRNA
   c. ribosome and mRNA . . . a gene and a tRNA
   d. gene and tRNA . . . a ribosome and an mRNA
   e. tRNA and ribosome . . . a gene and an mRNA

8. A sequence of pictures of polypeptide synthesis shows a ribosome holding two transfer RNAs. One tRNA has a polypeptide chain attached to it; the other tRNA has a single amino acid attached to it. What does the next picture show?
   a. The polypeptide chain moves over and bonds to the single amino acid.
   b. The tRNA with the amino acid leaves the ribosome.
   c. The amino acid moves over and bonds to the polypeptide chain.
   d. The tRNA with the polypeptide chain leaves the ribosome.
   e. A third tRNA with an amino acid joins the pair on the ribosome.

9. A microbiologist analyzed chemicals obtained from an enveloped RNA virus (similar to a mumps virus) that infects monkeys. He found that the virus envelope contained a protein characteristic of monkey cells. Which of the following is the most likely explanation for this?
   a. The virus gets its envelope when it leaves its host cell.
   b. The virus forced the monkey cell to make proteins for its envelope.
   c. The virus has a lysogenic life cycle.
   d. The virus gets its envelope when it enters its host cell.
   e. The virus fools its host cell by mimicking its proteins.

10. At one point as a cell carried out its day-to-day activities, the nucleotides G A T were paired with the nucleotides C U A. This pairing occurred
    a. in a double-stranded DNA molecule.
    b. during translation.
    c. during transcription.
    d. when an RNA codon paired with a tRNA anticodon.
    e. It is impossible to say, given this information.

11. Which of the following does not take part in polypeptide synthesis?
    a. an exon
    b. mRNA
    c. an intron
    d. tRNA
    e. a ribosome

Essay

1. *E. coli* bacteria are used in many genetic studies. Type A *E. coli* can live on a simple nutrient medium, because they have all the genes necessary to produce the chemicals they need. Type V *E. coli* can live only on a nutrient medium to which a certain vitamin has been added, because they lack a gene that enables them to make this vitamin for themselves. It has been found that bacteria can absorb genes from other dead, ground-up bacteria. Describe an experiment using type A and type V *E. coli* to determine whether genes are made of protein or DNA.
2. It is possible to extract DNA from cells and analyze it to determine the relative amounts of the four DNA bases. The DNA of a goldfish contains more T and less G than human DNA, but in both goldfish and human DNA the amount of T is equal to the amount of A. Explain why.
3. Eric said to Renee, "The amino acid sequence of the proteins in your hair determines how curly or straight your hair will be." Renee replied, "I don't think that's right. Your genes determine whether your hair is curly or straight. That's why it's inherited." Who is right? Explain.
4. The DNA base sequence for a short gene is:

   TATGATACCTTGATAGCTATCTGATTG.

   What is the amino acid sequence of the polypeptide produced according to this DNA information? Use the genetic code chart (Figure 10.8A in the text) and your knowledge of transcription and translation to figure out the message.
5. A biochemist found that a bacterium produced an mRNA molecule consisting of 852 nucleotides and translated this mRNA into a polypeptide containing 233 amino acids. How many nucleotides in the mRNA message would actually be needed to carry the message for the polypeptide, and how many were "extras"? How would the bacterium know *which* nucleotides made up the message?
6. The virus that causes chickenpox can disappear for years and then reappear in a line of painful sores ("shingles") where a nerve cell passes through the skin. How can viruses go away and then reappear like this? Where are the viruses during the intervening period of time?
7. A gene can be removed from a eukaryotic cell and spliced into the DNA of a prokaryotic cell. The prokaryotic can transcribe the gene into mRNA and translate this mRNA into a polypeptide, but the polyeptide has an incorrect amino acid sequence, very different from the polypeptide normally produced by the eukaryotic cell. Why?

Extending Your Knowledge

1. One of the most important things you can learn in your study of biology is how to keep from becoming infected with HIV, the AIDS virus. Information is available from college health centers and the CDC National STD AIDS Hotline, 1-800-342-AIDS.
2. In recent years, there have been several major outbreaks of "childhood" viral diseases such as measles on college campuses. Most young children are vaccinated, so unvaccinated individuals are not likely to contract these diseases "naturally." Unfortunately, these viruses can have serious effects, especially on adults. Do you know whether you have been vaccinated for measles, mumps, chickenpox, and so on? Did you have any of these diseases when you were younger? Your family or family doctor may have information about this. If you are not immune to these diseases, you may want to ask your doctor or college health center about vaccination.