Chapter 9: DNA: The Molecule of Heredity

OVERVIEW

In this chapter, you will learn about the molecular basis of inheritance, namely DNA. The authors describe the structure of DNA and explain how DNA makes accurate copies of itself. Melanoma is a relatively common skin cancer that begins in pigmented cells of the lower parts of the skin. Melanoma can spread to other body organs, frequently leading to death. The frequency of melanoma is increasing, and often is caused by increased exposure to sunlight, which can cause changes in the genetic material.

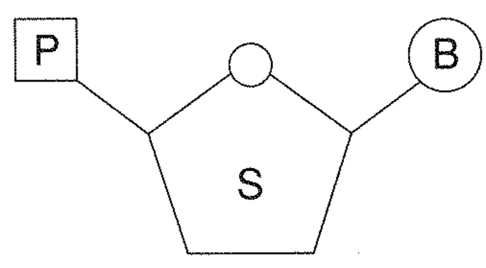
1) How Did Scientists Discover that Genes Are Made of DNA?

Fifty years ago, no one knew that deoxyribonucleic acid, or **DNA**, is the molecule that carries the blueprints for all forms of life on Earth. DNA enables organisms and their cells to transmit information accurately from one generation to the next. Learning DNA's structure and how it worked required the incremental advances of dozens of scientists working for decades. Starting in the late 1800s, scientists learned that heritable information exists in discrete units called **genes**. Studies of dividing cells provided strong evidence that genes are located in **chromosomes**, which are made of both DNA and **protein**, indicating that genes are made of either DNA or protein. Experiments using bacteria eventually provided clear proof that genes are made of DNA.

Transformed bacteria revealed the link between genes and DNA. In the 1920s Griffith was trying to make a vaccine to prevent pneumonia infections, using two strains of *Streptococcus pneumonia* bacteria. The R-strain did not cause pneumonia when injected into mice, and the S-strain caused pneumonia. Heat killed S-strain bacteria did not cause disease. He mixed living R-strain with heat-killed S-strain bacteria, and injected them into mice, which sickened and died, yielding living S-strain bacteria from their organs. Some substance in the heat-killed S-strain transformed the living, harmless R-strain into a deadly S-strain. Later, Avery, MacLeod, and McCarty purified the molecules from the S-strain bacteria that could transform the R-strain into a deadly S-strain. The transforming molecules were DNA.

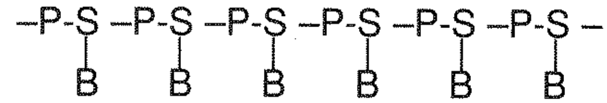
2) What Is the Structure of DNA?

DNA is made of four types of small subunits called **nucleotides**, each with a sugar (S) called deoxyribose, a phosphate group (P), and one of four possible nitrogen-containing **bases** (B): **adenine** (A), **thymine** (T), **guanine** (G), or **cytosine** (C).



In the 1940s, Chargaff discovered that the DNA of any species contains equal amounts of adenine and thymine, as well as equal amounts of cytosine and guanine. Wilkins and Franklin used X-ray diffraction to study DNA structure, finding that the molecule is helical (twisted like a corkscrew), has a uniform diameter (2 nanometers), and consists of repeating subunits.

Watson and Crick suggested that a DNA molecule consists of two DNA **strands** of linked nucleotides. Within each DNA strand, the phosphate group of one nucleotide bonds to the sugar of the next, producing a "backbone" of alternating, covalently bonded sugars and phosphates. The bases protrude from the **sugar-phosphate backbone**.



Watson and Crick said that hydrogen bonds between complementary bases hold the DNA strands together. Hydrogen bonds form between the protruding bases of the two separate DNA **strands**, giving DNA a ladder-like structure with the sugar-phosphate backbones on the outside and the nucleotide bases on the inside. The DNA strands are twisted about each other to form a **double helix**, like a ladder twisted lengthwise into a circular staircase. In the double helix, the two DNA strands are oriented in opposite directions. At each end of the double helix, one DNA strand ends with a free phosphate and the other ends with a free sugar. Within DNA, adenine forms hydrogen bonds only with thymine, and guanine forms bonds only with cytosine. These A-T and G-C linkages are called **complementary base pairs**, and explain Chargaff's results.

It is not the number of different subunits, but their order that is important. The order of nucleotides in DNA can encode vast amounts of information. Within a DNA strand, the four types of bases can be arranged in any linear order, with each sequence representing a unique set of genetic instructions, like a biological Morse code. A stretch of DNA just 10 nucleotides long can have more than a million possible sequences of the four bases, and a typical plant or animal chromosome has billions of nucleotides.

3) How Does DNA Replication Ensure Genetic Constancy?

DNA replication produces two DNA double helices, each with one old strand and one new strand. Each chromosome has a single long DNA double helix together with proteins that help organize and fold up the DNA. DNA duplication (replication) produces two identical double helices of DNA, each of which will be passed, within its chromosome, to one of the new daughter cells. DNA replication begins when enzymes pull the parental DNA double helix apart, so that the parental strands no longer form base pairs with each other. Other enzymes move along each separated DNA strand, selecting free nucleotides with complementary bases to the parental strand. The enzymes join these **free nucleotides** together to form two new DNA strands, each complementary to one of the original parental strands. When replication is complete, one original strand and one new complementary strand wind together into one double helix. The other original strand and new complementary strand do likewise. This process is called **semiconservative replication**. The new double helices are held together while the cell prepares for division. The chromosome at this stage is called a duplicated chromosome with two "sister" chromatids.

More details of the process follow. **DNA helicase** (an enzyme that breaks apart the helix) separates the parental DNA strands, using ATP energy to break the hydrogen bonds between complimentary base pairs. This activity separates and unwinds the parental DNA double helix, forming a **replication "bubble"** containing two replication "forks" where the two parental DNA strands have not yet unwound. In eukaryotic cells, many replication bubbles occur simultaneously on each chromosome to speed up the process. The bubbles grow and meet up.

DNA polymerase (an enzyme that makes a DNA polymer) makes new DNA strands. At each replication fork, DNA polymerase makes two new DNA strands that are complementary to the two parental strands by matching up unpaired parental bases with free nucleotides with the correct complementary bases. Then DNA polymerase catalyzes formation of new covalent bonds that link the phosphate of the incoming free nucleotide to the sugar of the previously added one, making the sugar-phosphate backbone of the daughter strand.

DNA polymerase can only add new nucleotides onto the free sugar end of the new DNA strand that it is making. But the two strands of the parental DNA molecule are oriented in opposite directions. So, as

DNA helicase separates parental strands, one DNA polymerase moves in the same direction as the helicase, adding nucleotides to form a long continuous daughter DNA strand. The second DNA polymerase must move in the opposite direction, making a daughter strand in small discontinuous segments. These segments are subsequently connected by **DNA ligase**. DNA ligase also plays a role in repairing DNA damaged by sunlight.

Proofreading produces almost error-free replication of DNA. Nearly 700 nucleotides per second are replicated by DNA polymerase, leading to an error about once in every 10,000 base pairs. But most of these errors are repaired by a variety of DNA repair enzymes that "proofread" each daughter strand during and after it is made and make any necessary repairs. Ultimately, the completed DNA strands contain about one mistake in every billion base pairs. But these mistakes do happen. Also, the DNA in each human cell loses about 10,000 base pairs daily by spontaneous chemical breakdown due to our body temperature of 98.6° F. Environmental agents, like ultraviolet radiation, also can damage DNA. Deterioration in the accuracy of DNA replication as people get older may contribute to the aging process.

Case study revisited. Thymine and cytosine are particularly prone to UV damage. Two adjacent thymines in a DNA strand can be improperly linked together by UV radiation. Unless the damage is repaired, DNA polymerase may be unable to properly replicate this region of DNA and may insert incorrect nucleotides into the daughter strand. If the involved gene controls cell division, it may lead to skin cancer. When you get a sunburn, many skin cells sustain more damage than can be repaired, and the cells die and peel off. Less damaged cells are repaired, but people who lack functional repair enzymes needed to repair UV-damage can have a variety of disorders, including xeroderma pigmentosum, being very sensitive to sunlight and prone to cancer. Getting sunburned as a child raises the risk of developing melanoma about three-fold. Recognizing a melanoma is as easy as ABCD: look for moles with Asymmetry, irregular Border, irregular Color, or a Diameter larger than the eraser at the end of a pencil.

KEY TERMS AND CONCEPTS

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

AATC	cytosine	GC and AT	helicase	nucleotides
adenine	DNA	GTTAC	helix	polymerase
chromosomes	four	guanine	ligase	semiconservative

1. Genes are made of molecules of ________________ which is made of ________________ that have a phosphate group, a sugar, and a nitrogenous base. The genetic molecule has a double-_______________ 3-dimensional structure.

2. There are ________________ different bases that are used to build a DNA molecule.

3. _________________ is the base that pairs with thymine, _________________ is the base that pairs with guanine, and _______________________ is the base that pairs with cytosine in DNA. Therefore, __________________ are complementary base pairs.

4. DNA replication is _____________________.

5. __________________ is the enzyme that unwinds DNA during replication. New strands of DNA are made using the enzyme _____________________, and __________________ is the enzyme that connects the short segments of nucleotides in a newly made DNA strand.

6. The complimentary base sequence for TTAG is ____________________ and the complementary base sequence for CAATG is ____________________

7. ____________________ are the cell structures in the nucleus that contain the genetic material.

Key Terms and Definitions

adenine: a nitrogenous base found in both DNA and RNA; abbreviated as *A*.

base: in molecular genetics, one of the nitrogen-containing, single- or double-ringed structures that distinguish one nucleotide from another. In DNA, the bases are adenine, guanine, cytosine, and thymine.

chromosome (krō´-mō-sōm): a single DNA double helix together with proteins that help to organize the DNA.

complementary base pair: in nucleic acids, bases that pair by hydrogen bonding. In DNA, adenine is complementary to thymine and guanine is complementary to cytosine; in RNA, adenine is complementary to uracil, and guanine to cytosine.

cytosine: a nitrogenous base found in both DNA and RNA; abbreviated as C.

deoxyribonucleic acid (dē-ox-ē-rī-bō-noo-klā´-ik; DNA): a molecule composed of deoxyribose nucleotides; contains the genetic information of all living cells.

DNA helicase: an enzyme that helps unwind the DNA double helix during DNA replication.

DNA ligase: an enzyme that joins the sugars and phosphates in a DNA strand to create a continuous sugar-phosphate backbone.

DNA polymerase: an enzyme that bonds DNA nucleotides together into a continuous strand, using a preexisting DNA strand as a template.

DNA replication: the copying of the double-stranded DNA molecule, producing two identical DNA double helices.

double helix (hē´-liks): the shape of the two-stranded DNA molecule; like a ladder twisted lengthwise into a corkscrew shape.

free nucleotides: nucleotides that have not been joined together to form a DNA or RNA strand.

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.

guanine: a nitrogenous base found in both DNA and RNA; abbreviated as *G*.

nucleotide: a subunit of which nucleic acids are composed; a phosphate group bonded to a sugar (deoxyribose in DNA), which is in turn bonded to a nitrogen-containing base (adenine, guanine, cytosine, or thymine in DNA). Nucleotides are linked together, forming a strand of nucleic acid, as follows: Bonds between the phosphate of one nucleotide link to the sugar of the next nucleotide.

protein: polymer of amino acids joined by peptide bonds.

replication bubble: the unwound portion of the two parental DNA strands, separated by DNA helicase, in DNA replication.

semiconservative replication: the process of replication of the DNA double helix; the two DNA strands separate, and each is used as a template for the synthesis of a complementary DNA strand. Consequently, each daughter double helix consists of one parental strand and one new strand.

strand: a single polymer of nucleotides; DNA is composed of two strands.

sugar-phosphate backbone: a major feature of DNA structure, formed by attaching the sugar of one nucleotide to the phosphate from the adjacent nucleotide in a DNA strand.

thymine: a nitrogenous base found only in DNA; abbreviated as *T*.

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.

8. _____ A molecule of DNA is <u>single</u> stranded.

9. _____ DNA contains four types of <u>sugars</u>.

10. _____ Sugars found in DNA have <u>five</u> carbons each.

11. _____ DNA is found in cellular <u>chromosomes</u>.

12. _____ DNA contains sugars, bases, and <u>sulfur</u> groups.

13. _____ The concentration of DNA is <u>constant</u> for different body cells of the same species.

14. _____ Adenine pairs with <u>guanine</u> in DNA.

15. _____ The duplication of DNA is called <u>fully</u> conservative replication.

16. _____ The building blocks of nucleic acids are <u>amino acids</u>.

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

17. If amounts of bases in a DNA molecule are measured, we find
    a. A = C and G = T
    b. A = G and C = T
    c. T = A and C = G
    d. that no two bases would be equal in amount
    e. that all bases are equal in amount

18. The DNA of a certain organism has guanine as 30% of its bases. What percentage of its bases would be adenine?
    a. 0
    b. 10%
    c. 20%
    d. 30%
    e. 40%

19. The correct structure of a nucleotide is
    a. phosphate–ribose–adenine
    b. phospholipid–sugar–base
    c. phosphate–sugar–phosphate–sugar
    d. adenine–thymine and guanine–cytosine
    e. phosphate–sugar–base

20. The two polynucleotide chains in a DNA molecule are attracted to each other by
    a. covalent bonds between carbon atoms
    b. hydrogen bonds between bases
    c. peptide bonds between amino acids
    d. ionic bonds between "R" groups in amino acids
    e. covalent bonds between phosphates and sugars

21. Using an analogy of DNA as a twisted ladder, the rungs (steps) of the ladder are
    a. phosphate groups
    b. sugar groups
    c. paired nitrogenous bases
    d. oxygen-carbon double bond

22. All the cells of a specific organism contain equal amounts of
    a. adenine and guanine
    b. guanine and cytosine
    c. adenine and cytosine
    d. thymine and cytosine

23. The sequence of subunits in the DNA backbone is
    a. –base–phosphate–sugar–base–phosphate–sugar–
    b. –base–phosphate–base–phosphate–base–phosphate–
    c. –phosphate–sugar–phosphate–sugar–phosphate–sugar–
    d. –sugar–base–sugar–base–sugar–base–sugar–base–
    e. –base–sugar–phosphate–base–sugar–phosphate–

24. Figuratively speaking, a double helix is comparable to
    a. coiled rope
    b. stacked up plates
    c. braided hair
    d. twisted ladder
    e. tangled threads

25. Melanoma is a cancer caused by exposure to
    a. X rays
    b. harmful chemicals
    c. sea water
    d. ultraviolet radiation
    e. skin cream

26. Excessive amounts of sunlight will cause which adjacent DNA bases to form improper bonding?
    a. adjacent thymine bases
    b. adjacent adenine bases
    c. adjacent cytosine bases
    d. adjacent guanine bases
    e. any pair of adjacent bases

27. The genetic condition "xeroderma pigmentosum" occurs due to the lack of which functional enzymes?
    a. DNA polymerase
    b. DNA repair enzymes
    c. DNA ligase
    d. DNA helicase
    e. DNA replicase

28. Getting severely sunburned as a child raises the risk of developing melanoma later in life about three-fold.
    a. true
    b. false

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.

29. Instead of DNA being a double-stranded molecule, suppose DNA was a single-stranded molecule, so that each complete molecule of DNA consisted of one chain of nucleotides. If DNA were single-stranded, describe how DNA replication could take place, using the same DNA polymerase enzyme that creates complimentary base pairing, so that exact copies of genes could be made. Would this be more efficient or less efficient than replication involving double-stranded DNA? Briefly explain.

30. Look at figure 9.3 in your textbook. Can you briefly explain why cytosine can pair only with guanine, and not with adenine or thymine?

31. Analysis of the relative amounts of the four types of bases in DNA from tuberculosis bacterium shows that it contains roughly 15% adenine, 15% thymine, 35% cytosine, and 35% guanine. A similar analysis of human DNA shows more adenine (30%) and thymine (30%), and less cytosine (20%) and guanine (20%). However, both human DNA and tuberculosis bacterial DNA contain 50% of the one-ring bases thymine and cytosine, and 50% of the two-ring bases adenine and guanine. Explain the differences and similarities of the DNA from the two sources.

32. Suppose a genetic transformation experiment is performed between two types of bacteria, where one strain (strain A) can make its own vitamin B_6 due to the presence of an active gene, and the other strain (strain B) cannot make its own vitamin B_6 due to the presence of a defective gene. Describe an experiment that might determine whether genes are made of DNA or of proteins.

33. In DNA molecules, when base pairing occurs between adenine and thymine, two hydrogen bonds form between them. However, when base pairing occurs between cytosine and guanine, three hydrogen bonds form between them. Let's say that we compared DNA from two different species. Species A's DNA has 40% A-T base pairs and 60% G-C base pairs, while Species B's DNA has 70% A-T base pairs and 30% G-C base pairs. Which type of DNA would have to be heated to a higher temperature in order to get the double stranded DNA to dissociate into single strands?

34. Suppose someone presented data from an analysis of the DNA of a newly discovered species showing that the relative amounts of the DNA bases were 30% for adenine, 30% for guanine, 20% for thymine, and 20% for cytosine. In what ways would these data not make sense in relation to what we know about the structure of DNA?

35. Predict the complementary base sequence for each of the following short DNA molecules. Also predict which molecule would be more stable at a temperature 15 degrees above normal body temperature.

Molecule One: 5'-CGTAGTAGTAGAATATTGCTGCACC-3'

Molecule Two: 5'-AGTGCGAAGGCTCCTTGGGAACGTG-3'

36. Suppose one strand of a DNA molecule contains the following proportions of bases: 10% T, 20% A, 30% C, and 40% G. What proportions of the four types of bases would you expect in the double-stranded form of this DNA molecule?

37. What are the things to look for when examining your skin for the presence of melanoma cancer?