# **DNA Structure and** Replication

This baby goat literally gets its looks from its mother, thanks to cloned DNA.

**Gather Evidence** Ξ

6.1

As you explore the lesson, gather evidence to explain how scientists determined the function and structure of DNA.

#### **CAN YOU EXPLAIN IT?**

How can you make conclusions about something you cannot see? This has been a challenge throughout the history of science. Sometimes scientists must use indirect evidence.

FIGURE 1: Each of these images shows a sample of DNA at a different level of detail.



Understanding the structure and function of DNA is one such case in biology. Early biologists recognized that characteristics were passed from one generation to the next, but the molecules responsible for this phenomenon were too small to be seen using early microscopes. Remarkably, biologists pieced together evidence about the structure of the molecule responsible for the unique characteristics of each organism. Over time, scientists built on the work of others, and, at the same time, technology continued to improve. Today, we have a much more clear understanding about DNAthe molecule that contains the code for life.

**Predict** Based on the images shown in Figure 1, how would you describe the appearance of DNA?

## The Function of DNA

You are one of a kind and like no other—unless you are an identical twin, of course! How is it that you are so unique? You have a set of traits, or distinguishing characteristics, such as hair color, eye color, face shape, and body type, that are passed from one generation to the next. Early scientists made these same observations. But a question remained: How are traits passed from one generation to the next?



**Analyze** As you can see in Figure 2, humans have many observable traits that set us apart from each other. What are some traits you have?

FIGURE 2: Unique traits are observable among humans.



## **Codes for Proteins**

DNA, or deoxyribonucleic acid, is the molecule that stores the genetic information for all organisms. DNA is heritable, which means it can be passed from parent to offspring. This explains why offspring may look like their parents and why individual organisms within a species share many of the same characteristics. Scientists understood that traits were heritable long before they identified DNA and its key role in inheritance.

DNA does not act alone to pass on genetic information. The information from DNA is used to build another nucleic acid called RNA, or ribonucleic acid, and RNA in turn builds proteins. This concept is known as the central dogma of molecular biology. Recall that proteins play a crucial role in body functions. Enzymes help regulate chemical reactions. Other proteins provide structural support for cells. Proteins in the cell membrane transport nutrients across the membrane in response to changing conditions inside or outside the cell. Each protein has a unique structure and function in the cell, so proper coding is critical for building each protein.

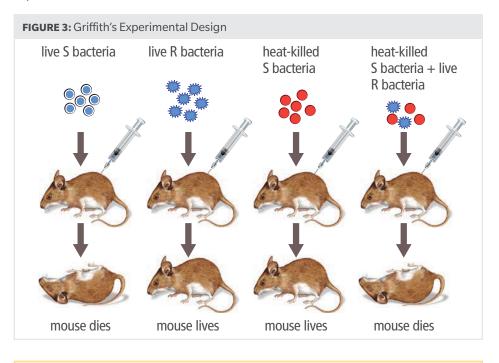
**Predict** Kinesin is a motor protein that transports organelles and proteins around a cell. The structure of kinesin is crucial for its function. What might happen to the structure of kinesin if the DNA code was damaged?

## Mechanism for Heredity

Genetics is the study of biological inheritance patterns and variation in organisms. Gregor Mendel, an Austrian monk, was an early contributor to our understanding of genetics. Mendel's revolutionary experimentation with breeding pea plants identified factors that controlled traits. He correctly predicted that traits can be inherited as discrete units passed from parents to offspring. However, it would take the work of several different scientists over many years to discover DNA and explain how it codes for the inheritance of individual traits. Results from experiments led by these scientists supported the conclusion that DNA is the molecule of inheritance.

### **Griffith's Experiments**

In 1928, the British microbiologist Frederick Griffith was investigating two types of pneumonia-causing bacteria. One type, called *S*, has a smooth outer coating made from carbohydrates. The other type, called *R*, has a rough outer surface. As shown in Figure 3, when Griffith injected mice with both types of bacteria, only the S–type killed the mice. When Griffith injected mice with heat–killed S bacteria, they were unaffected. However, when he injected the mice with a combination of heat–killed S bacteria and live R bacteria, the mice died. Even more surprising, he found live S bacteria in a blood sample taken from the dead mice. Unable to identify the factor that transformed harmless R bacteria into disease-causing S bacteria, Griffith called the mystery material the *transforming principle*. This mystery would be a question for other scientists to explore.



Analyze What evidence suggested that there is a transforming principle?

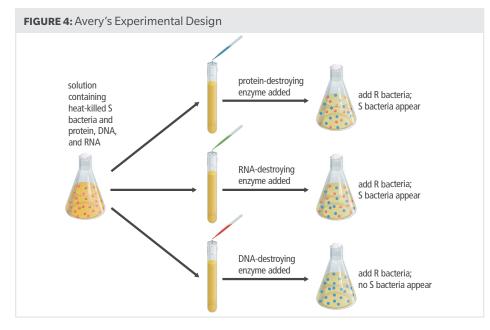
#### **Avery's Experiments**

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Oswald Avery and his fellow scientists were intrigued by Griffith's transforming principle. Avery's team worked for more than 10 years to answer the question of what transformed the R strain. The scientists started with heat-killed S bacteria cells. They used a detergent to break down the bacteria, which resulted in an extract that contained only protein, DNA, and RNA molecules. Initial experiments showed that this extract contained the transforming principle.

Avery's team then used enzymes to break down each of the molecules separately. Once degraded, each sample was mixed with R-strain bacteria to test for transformation to S-strain. The results of this work are shown in Figure 4.

**Collaborate** With a partner, discuss what further questions you would ask based on Griffith's experimental results.



Avery and his group performed a chemical analysis of the molecule determined to be the "transforming principle." The table in Figure 5 shows the percentage of nitrogen and phosphorus and the ratio of nitrogen to phosphorus for four samples.

## Data Analysis

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FIGURE 5: Chemical analysis of the transforming principle						
	% Nitrogen (N)	% Phosphorus (P)	Ratio of N to P			
Sample A	14.21	8.57	1.66			
Sample B	15.93	9.09	1.75			
Sample C	15.36	9.04	1.69			
Sample D	13.40	8.45	1.58			
Known value for DNA	15.32	9.05	1.69			

**Analyze** How does the data in the table support the claim that DNA is the transforming principle?

Avery's group also performed standard chemical tests that showed DNA was present in the extract and protein was not. They also used enzymes to destroy different molecules such as lipids and carbohydrates. Each time a molecule was destroyed, the transformation from R to S bacteria still occurred—until they destroyed DNA. When DNA was destroyed, the transformation did not occur.

In 1944, Avery and his group presented the evidence to support their conclusion that DNA must be the transforming principle, or genetic material. However, the scientific community remained skeptical as to whether the genetic material in bacteria was the same as that in other organisms. Despite Avery's evidence, some scientists insisted that his extract must have contained protein. Further testing remained to be done.

**Explain** Why did Avery's group destroy each type of molecule before adding it to the solution containing R bacteria? What can you conclude from the results?

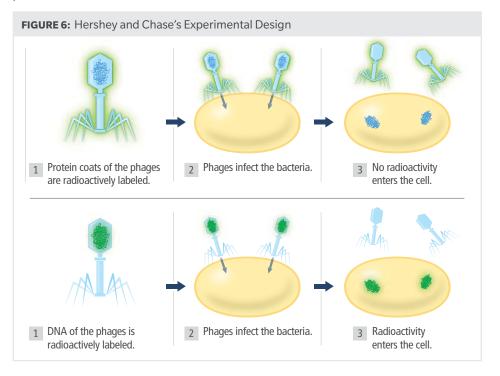
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### **Hershey and Chase Experiments**

In 1952, two American biologists, Alfred Hershey and Martha Chase, were researching different viruses that infect bacteria. These viruses, called bacteriophages, are made up of a DNA core surrounded by a protein coat. To reproduce, the bacteriophages attach themselves to bacteria and then inject material inside the cell. Hershey and Chase thought up a clever procedure that used the chemical elements found in protein and DNA. Protein contains sulfur but very little phosphorus, while DNA contains phosphorus but no sulfur. The researchers grew phages in cultures that contained radioactive isotopes of sulfur or phosphorus. Hershey and Chase then used these radioactively tagged phages in two experiments.

In the first experiment, bacteria were infected with phages that had radioactive sulfur atoms in their protein molecules. Hershey and Chase then used a kitchen blender and a centrifuge to separate the bacteria from the parts of the phages that remained outside the bacteria. When they examined the bacteria, they found no significant radioactivity.

In the second experiment, Hershey and Chase repeated the procedure with phages that had DNA tagged with radioactive phosphorus. This time, radioactivity was clearly present inside the bacteria.



E Analyze Why did the Hershey and Chase experiments support the idea that DNA is the transforming principle?

Explain

- 1. Draw a table to summarize each experiment. Include information on how the experiments relate to one another, key data, and questions that remained after each experiment.
- 2. Develop an argument for why the data from each experiment either supported or did not support the conclusion that DNA is the molecule of inheritance.
- **3.** Scientists often build on, and improve, the work of other scientists. This process may cover a long period of time. Explain how advances in technology affect this process of building scientific knowledge.

## The Structure of DNA

Once Hershey and Chase completed their experiments with bacteriophages, it was clear that DNA was responsible for the inheritance of traits. What scientists did not yet understand, however, was how DNA stored genetic information. To understand this, they first needed to understand the molecular structure of DNA.

## Nucleotides

Scientists have known since the 1920s that the DNA molecule is a very long polymer, or chain of repeating subunits. The subunit, or monomer, that makes up DNA is called a nucleotide, shown in Figure 7.

One molecule of human DNA contains billions of nucleotides. However, if you were to divide all of those nucleotides into groups of identical nucleotides, you would end up with just four groups. The nucleotides that make up DNA differ only in their nitrogen–containing, or nitrogenous, bases. The bases are cytosine (C), thymine (T), adenine (A), and guanine (G). The letter abbreviations refer both to the bases and to the nucleotides that contain the bases.

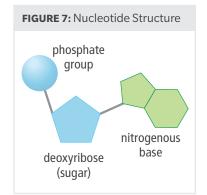


FIGURE 8: The four nucleotides that make up DNA

PYRIMIDINES			PURINES			
	Name of base	Structural formula	Model	Name of base	Structural formula	Model
	thymine		T	adenine	HC N NH2 HN C N CH	A
	cytosine		С	guanine	HC N HN C NH NH2	G

c | c |

**Explain** Use the information in Figure 8 to answer the following questions.

- 1. How do the structures of purines differ from the structures of pyrimidines?
- 2. Which base is most similar in structure to thymine?

## **Determining DNA Structure**

For a long time, scientists assumed that DNA was made up of equal amounts of the four nucleotides and that the DNA in all organisms was therefore exactly the same. That assumption made it difficult to convince scientists that DNA was the genetic material. They reasoned that identical molecules could not carry different instructions across all organisms. However, in 1950, Erwin Chargaff conducted a set of experiments that challenged this assumption.

## **Chargaff's Experiments**

Chargaff changed the thinking about DNA by analyzing the DNA of several different organisms. He found that the same four bases are found in the DNA of all organisms, but the proportion of the four bases differs from one organism to another.

## Data Analysis

FIGURE 9: Nucleotide ratios leading to the formulation of Chargaff's rules

Source	Adenine to Guanine	Thymine to Cytosine	Adenine to Thymine	Guanine to Cytosine	Purines to Pyrimidines
Human	1.56	1.75	1.00	1.00	1.00
Chicken	1.45	1.29	1.06	0.91	0.99
Salmon	1.43	1.43	1.02	1.02	1.02
Wheat	1.22	1.18	1.00	0.97	0.99
Yeast	1.67	1.92	1.03	1.20	1.00
E-coli k2	1.05	0.95	1.09	0.99	1.00

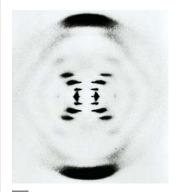
## Analyze

- 1. The numbers shown in the table are ratios. For example, the ratio of adenine to guanine in humans is 1.56 to 1, or 1.56:1. The 1 is assumed, and not shown. What do you observe about these ratios?
- **2.** How does Chargaff's work support the idea that DNA is the molecule of inheritance?

#### FIGURE 10: X-ray Evidence



a Rosalind Franklin



**b** X-ray crystallography

### Franklin's X-Ray Crystallography

In the early 1950s, British scientist Rosalind Franklin was studying DNA using a technique called x-ray crystallography. When crystallized DNA is bombarded with x-rays, the atoms diffract the x-rays in a pattern that can be captured on film. Franklin's x-ray photographs of DNA showed an X surrounded by a circle. The pattern and angle of the X suggested that DNA consists of two strands, spaced at a consistent width apart and twisted into a helical shape.

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**Collaborate** Rosalind Franklin's results made her think that the DNA molecule was a helical, or spiral, shape. With a partner, discuss what questions about the structure of DNA were not answered by her results.

## Watson and Crick's Model of DNA

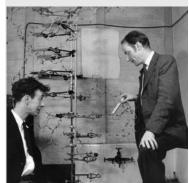
At about the same time that Franklin was working with x-ray crystallography, American geneticist James Watson and British physicist Francis Crick were also studying DNA structure. Their interest was sparked by the earlier work of Hershey, Chase, and Chargaff as well as biochemist Linus Pauling. Pauling discovered that the structure of some proteins was a helix, or spiral. Watson and Crick hypothesized that DNA might also be a helix. Franklin's crystallographs, along with her calculations, gave them the clues they needed to develop models like the one shown in Figure 11.

Watson and Crick began working with their model to determine the structure of DNA. They knew they had to be able to twist their model to account for the evidence provided by Franklin's x-rays. They placed the sugar-phosphate backbones on the outside and the nitrogenous bases on the inside. At first, Watson reasoned that A might pair with A, T with T, and so on. But the bases A and G are about twice as wide as C and T, so this made a helix that varied in width. This arrangement was not supported by Franklin's data, which showed that the width of the molecule was constant. Finally, Watson and Crick found that if they paired doubled-ringed nucleotides with single-ringed nucleotides, the bases fit like a puzzle.

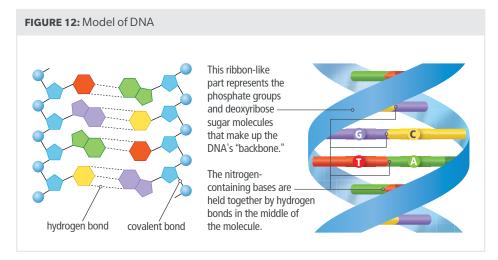
In April 1953, Watson and Crick published their DNA model in the journal *Nature*. Working from Franklin's data, they built a double-helix model in which the two strands were complementary—that is, if one strand is ACACAC, the other strand is TGTGTG. The pairing of bases in their model supported Chargaff's results. These A–T and C–G relationships became known as Chargaff's rules.

## Current DNA Model

As technology has advanced, our understanding of DNA has continually improved. The current model represents DNA nucleotides of a single strand joined together by covalent bonds that connect the sugar of one nucleotide to the phosphate of the next nucleotide. The alternating sugars and phosphates form the sides of a double helix, or the sugar-phosphate backbone of the molecule. The DNA double helix is held together by hydrogen bonds between the bases in the middle. Individually, each hydrogen bond is weak, but together, they maintain DNA structure. **FIGURE 11:** James Watson (left) and Frances Crick (right) used a model to figure out the structure of DNA.



Analyze By building a physical model, Watson and Crick were able to see that adenine fit with thymine and guanine fit with cytosine. How do Chargaff's results support Watson and Crick's model?



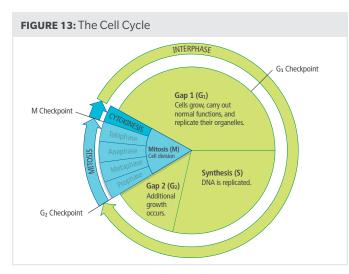
**Predict** Look at the hydrogen bonds between the base pairs in Figure 12. Which base pairs do you think are held more tightly together?

As Watson and Crick's model showed, the bases of the two DNA strands always follow Chargaff's rules for base pairing: thymine (T) always pairs with adenine (A), and cytosine (C) always pairs with guanine (G). These pairings occur because of the sizes of the bases—a purine is always paired with a pyrimidine—and the ability of the bases to form hydrogen bonds with each other. As an example of base pairing, if a sequence of bases on one strand of DNA is CTGCTA, the matching DNA strand will be GACGAT.



**Model** Describe the structure of DNA using a ladder as an analogy. What makes up the rungs, or steps, of the ladder? What makes up the sides? How is the ladder shaped?

## **DNA Replication**



**Explain** The word synthesis comes from a Greek word meaning "to put together, or combine." Why is the S phase called the synthesis phase?

#### Structure and Function

The name of an enzyme can explain its function. The suffix *-ase* indicates that a protein is an enzyme. The root word before the suffix indicates which molecule is the substrate for this enzyme. One enzyme involved in DNA replication is called helicase. The process by which DNA is copied during the cell cycle is called replication. This process takes place in the nucleus during the S phase of the cell cycle. After the two strands of DNA are separated, each strand becomes a template for a new strand of DNA. The order of the bases is preserved, so DNA is replicated accurately each time. Replication ensures that every cell has a complete set of identical genetic information.

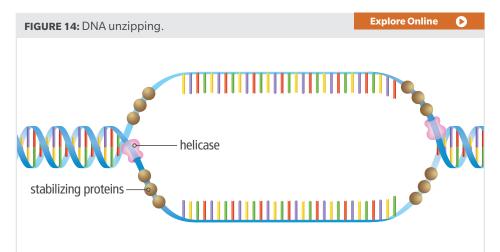
## **DNA Process for Replication**

DNA stores genetic information; however, it does not copy itself. Enzymes and other proteins do the work of replication. Some enzymes start the process by breaking the weak hydrogen bonds that hold the base pairs together. This

"unzips" the DNA molecule into two separate strands. Other proteins hold the strands apart while each strand serves as a template. Nucleotides that are floating free in the nucleus can then pair up with the nucleotides of the templates on each strand of the separated DNA. A group of enzymes called DNA polymerases are involved in this process. DNA polymerase binds the new nucleotides together. When the process is finished, the result is two complete molecules of DNA, each exactly like the original double strand.

#### **DNA Unzips**

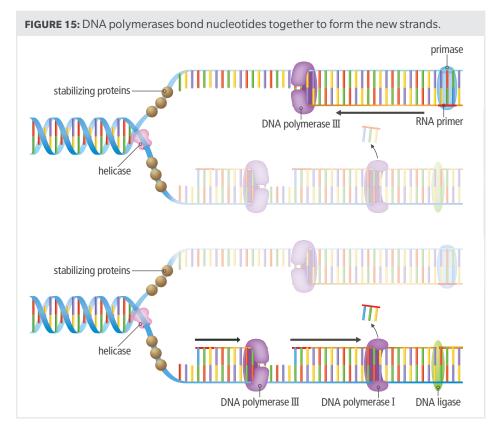
An enzyme called helicase binds to the DNA molecule and unzips the strands. This occurs at many places along the chromosome, called the *origins of replication*. The hydrogen bonds connecting base pairs are broken, the original molecule separates, and the bases on each strand are exposed. Other proteins, called stabilizing proteins, bind to and stabilize the separated strands. The process of unzipping DNA proceeds in two directions simultaneously, rather like unzipping a suitcase.



## **Nucleotide Pairing**

Once the DNA is unzipped, the process of adding nucleotides to the single-stranded templates begins. An enzyme called *primase* makes an RNA primer, a short nucleotide segment that begins the synthesis process. The RNA primer segment is necessary because DNA polymerase can only add nucleotides to an existing strand.

Similar to the unzipping process, replication takes place at both forks simultaneously. One by one, free nucleotides pair with the bases exposed as the template strands unzip. Starting at the primer, DNA polymerases bond the nucleotides together and form new strands using DNA nucleotides that are complementary to each template. Because the two strands of the DNA molecule are positioned in opposite directions, there are differences in how each strand is copied. On the *leading strand*, highlighted in the top image in Figure 15, DNA replication begins at the primer and proceeds in one direction as *DNA polymerase III* adds new nucleotides. On the *lagging strand*, highlighted in the bottom image in Figure 15, replication occurs in a discontinuous, piece-by-piece way in the opposite direction. On the lagging strand, primers attach at multiple locations so multiple molecules of DNA polymerase III can add nucleotides to each primer at the same time.



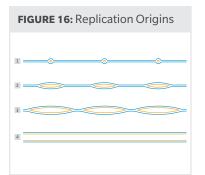
Once the open regions on both strands are filled in, an enzyme called *DNA polymerase I* removes the RNA primers from both strands and replaces them with DNA nucleotides. On the lagging strand, the fragments are then bound together by an enzyme called *ligase*.

When replication is complete, there are two identical molecules of DNA. Each molecule contains one strand of DNA from the original molecule and one new strand. This type of replication is called *semiconservative* because each new molecule of DNA conserves, or keeps unchanged, one strand of DNA from the original molecule.

Language Arts Connection Use an analogy to explain the sequence of events in the replication of DNA. Cite evidence from the diagram to support your explanation.

**Model** Make a model of a DNA molecule to explain semiconservative replication.

## Fast and Accurate Replication



In every living thing, DNA replication happens repeatedly, and it happens remarkably fast. In human cells, about 50 nucleotides are added every second to a new strand of DNA at an origin of replication. But even at this rate, it would take many days to replicate a molecule of DNA if the molecule were like a jacket zipper, unzipping one tooth at a time. To speed the process along, replication takes place at hundreds of origins of replication along the DNA molecule. This allows replication to be completed in only a few hours rather than days.

For the most part, replication proceeds smoothly. Occasionally, though, the wrong nucleotide is added to the new strand of DNA. This is called a *base substitution*, which is a type of point mutation—a mutation that occurs at a single location in the sequence of nucleotides. However, DNA polymerase can detect the error, remove the incorrect nucleotide, and replace it with the correct one. In this way, errors in DNA replication are limited to about 1 error per 1 billion nucleotides. If the substitution is not repaired, it may permanently change the organism's DNA. Sickle-cell anemia is an example of a genetic disorder that results from a base-substitution point mutation.



**Predict** Why is it important for DNA polymerase I to proofread the new strands of DNA before the cell divides?

## Engineering

#### FIGURE 17: Folded DNA Model



## The Art of DNA Folding

The human body has a knack for packing. It fits about eight meters of large and small intestines into the abdomen and jams about 100,000 kilometers of blood vessels, large and small, into the body. It should come as no surprise that the tiniest unit of the human body, the cell, has the same astonishing capability.

There are about 3 billion DNA base pairs in the human genome. If stretched out, the strand would be about 180 meters. This must fit into an area the size of a pinpoint. To make that happen, DNA must be tightly folded over and again, without becoming a tangled mess. The problem is solved by the formation of about 10,000 precise, non-overlapping loops like the ones in a bow. Instead of knots, the loops are held together by special proteins. The loops are crumpled to conserve space and are coated with chemical tags. The loops are then organized into groups by tag.





## **Extracting DNA**

While scientists use DNA extraction kits available from biotechnology companies, you can actually extract DNA using common ingredients found in your own home. During a DNA extraction, a detergent is used to burst open cells so that the DNA is released into solution. Then alcohol is added to the solution to cause the DNA to precipitate out. In this activity, you will extract DNA from a strawberry. Unlike human cells, which contain two copies of each chromosome, a strawberry has eight copies of each chromosome in its cells.



Predict What will DNA extracted from a strawberry look like?

#### PROCEDURE

- 1. Place the alcohol in a freezer 24 hours before beginning the lab.
- 2. Place the strawberry in a plastic zipper bag. Zip the bag closed.
- 3. Gently crush the strawberry by squeezing it inside the closed bag for 2 minutes.
- **4.** Carefully open the bag and add 1 teaspoon water, 1 teaspoon liquid dish soap, and a pinch of salt. Zip the bag closed. Knead for 1 minute.
- **5.** Pour the strawberry mixture into a cheesecloth-lined funnel that is set into a test tube to filter out the solids.
- 6. Remove the alcohol from the freezer. Open the test tube lid and tilt it in your hand. Very slowly, pour a small amount of alcohol down the inside of the test tube just until there is a thin layer floating on top of the solution.
- 7. Observe the test tube. You should see a band of white, gooey material forming just beneath the layer of alcohol. Gently put the skewer into the test tube and twirl it in the white material in one direction only. Wind the material around the skewer, then carefully draw it up and out of the test tube.
- 8. Record your observations.

#### ANALYZE

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**Explain** Use your results from this activity to answer the following questions.

- **1.** Describe the appearance of your DNA sample.
- 2. How is your DNA sample similar to and different from Watson and Crick's model?
- 3. The sample of DNA came from many strawberry cells. Do you think you would have been able to get the same result from your experiment if you had extracted DNA from a single cell?

#### EVIDENCE FOR DNA STRUCTURE AND FUNCTION

#### **TELOMERES AND AGING**

Go online to choose one of these other paths.

FIGURE 18: Strawberries have eight copies of each chromosome in their cells.



#### MATERIALS

- cheesecloth
- funnel
- isopropyl alcohol (91%)
- dish soap, liquid
- salt
- strawberry (1 per student)
- teaspoon
- test tube with stopper
- water
- wood skewer
- zipper bag, plastic, quart size



## Lesson Self-Check

### CAN YOU EXPLAIN IT?

FIGURE 19: With advanced technology, we can directly observe DNA.



The photos shown here represent images of DNA at different scales. Current models of DNA include specific details about the shape and chemical makeup of this molecule. How do we know what DNA looks like if even our best technology to date gives us limited images?

What we know about DNA today is the result of multiple scientists building on each other's work. At each step in the process, scientists made observations, asked questions, tested ideas, and shared data. Advances in technology let scientists expand on discoveries, adding new information to our body of knowledge. For example, Frederick Griffith's discoveries led to questions Oswald Avery wanted to answer. Avery's work, in turn, provided valuable information that helped Alfred Hershey and Martha Chase prove definitively that DNA is the molecule of inheritance. James Watson and Francis Crick built on Erwin Chargaff's base-pairing rules and evidence from Linus Pauling to propose DNA's helical structure. The work of Rosalind Franklin was critical to the confirmation that DNA did indeed have a twisted, helical shape.



**Explain** Refer to the notes in your Evidence Notebook to explain how you would describe the structure of DNA. Use evidence and models to support your explanation, and address the following questions in your explanation:

- 1. How did the research of scientists such as Chargaff, Franklin, Watson, and Crick help advance our understanding of the structure of DNA?
- 2. What other methods can you think of that could be used to further study the structure of an object, such as DNA?

### CHECKPOINTS

#### **Check Your Understanding**

- **1.** What is the complementary DNA strand for a strand with the nucleotide sequence AACCCGGTTT?
  - a. GGAAATTCCCT
  - **b.** TTAAACCGGG
  - c. TTGGGCCAAA
  - d. CCGGGTTAAT
- **2.** What did Avery's work on the identification of transforming factors prove?
  - a. DNA is made of four different nucleotides.
  - **b.** The DNA molecule is a double-stranded helix.
  - c. Genetic information is contained in DNA.
  - d. Bacterial DNA is interchangeable between species.
- **3.** Replication is a critical process during the cell cycle. In which phase of the cell cycle does replication take place?
  - **a.** G<sub>1</sub>
  - **b.** G<sub>2</sub>
  - **c.** S
  - **d.** M
- **4.** What knowledge did scientists gain based on the x-ray crystallograph taken by Rosalind Franklin?
  - a. The sequence of nucleotides
  - **b.** How nucleotide bases form a template
  - c. The role of DNA in genetic mutations
  - d. The double-helix structure of DNA
- **5.** How does the central dogma connect DNA, RNA, and proteins?
- **6.** What do you predict would happen to the length of a human pregnancy if there was a single origin of replication on each chromosome?
- **7.** What is the function of the proofreading step of replication? What might happen if this step were skipped?
- 8. What process did Watson and Crick use to develop their model of DNA, and how did it differ from the controlled experiments used by Griffith, Avery, and Hershey and Chase?

**9.** How do the base-pairing rules explain how a strand of DNA acts as a template during DNA replication?

### MAKE YOUR OWN STUDY GUIDE



In your Evidence Notebook, design a study guide that supports the main idea from this lesson:

## DNA codes for proteins and is responsible for an organism's traits.

Remember to include the following information in your study quide:

- Use examples that model main ideas.
- Record explanations for the phenomena you investigated.
- Use evidence to support your explanations. Your support can include drawings, data, graphs, laboratory conclusions, and other evidence recorded throughout the lesson.

Consider how the unique structure of DNA allows it to be copied and to transmit traits from parent to offspring.