Chapter 16: Molecular Basis of Inheritance

1. What are the two chemical components of chromosomes?

The two chemical components of chromosomes are DNA and protein.

2. Why did researchers originally think that protein was the genetic material?

Until the 1940s, biochemists though protein was the genetic material, as they had identified proteins as a class of macromolecules with great heterogeneity and specificity of function, essential requirements for hereditary material. Moreover, little was known about nucleic acids, whose physical and chemical properties seemed far too uniform to account for the multitude of specific inherited traits exhibited by every organism. The role of DNA in heredity was first worked out while studying bacteria and the viruses that infect them, which are far simpler than pea plants, fruit flies, or humans.

3. Distinguish between the virulent and nonvirulent strains of Streptococcus pneumoniae *studied by Frederick Griffith.*

Bacteria of the S (smooth) strain can cause pneumonia in mice; they are pathogenic because they have an outer capsule that protects them from an animal's defense system. Bacteria of the R (rough) strain lack a capsule and are nonpathogenic. To test for the trait of pathogenicity, Griffith injected mice with the two strains.

4. What was the purpose of Griffith's studies?

While attempting to develop a vaccine against pneumonia in 1928, Griffith explored the inheritance of pathogenicity.

5. Summarize the experiment in which Griffith became aware that hereditary information could be transmitted between two organisms in an unusual manner.

To test for pathogenicity, Griffith injected mice with pathogenic and nonpathogenic strains. Mice injected with the pathogenic control died while mice injected with nonpathogenic control remained healthy. Surprisingly, however, when the pathogenic bacteria were killed with heat and the cell remains then mixed with living cells of the nonpathogenic strain, some of the living cells became pathogenic, also killing the mice.

6. Define transformation.

Transformation is a change in genotype and phenotype due to the assimilation of external DNA by a cell. (This use of the term should not be confused with the conversion of a normal animal cell to a cancerous one.)

7. What did Oswald Avery determine to be the transforming factor? Explain his experimental approach.

Avery broke open the heat-killed pathogenic bacteria and extracted the cellular contents. He treated each of three samples with an agent that inactivated DNA, RNA, or protein, and then tested the sample for its ability to transform live nonpathogenic bacteria. Only when DNA was allowed to remain active did transformation occur.

8. Sketch a T2 bacteriophage and label its head, tail sheath, tail fiber, and DNA.

Bacteriophages are viruses that infect bacteria. Viruses are much simpler than cells. A virus is little more than DNA (or sometimes RNA) enclosed by a protective coat, which is often simply protein. To produce more viruses, a virus must infect a cell and take over the cell's metabolic machinery.

9. How does a bacteriophage destroy a bacterial cell?

First, the phage uses its tail fibers to bind to specific receptor sites on the outer surface of the bacterial cell. The sheath of the tail contracts, injecting the phage's DNA into the cell and leaving an empty capsid outside. The cell's DNA is hydrolyzed. The phage DNA then directs production of phage proteins and copies of the phage genome by host and viral enzymes, using components within the cell. Three separate sets of proteins self-assemble to form phage heads, tails, and tail fibers. The phage genome is packaged inside the capsid as the head forms. Finally, the phage directs production of an enzyme that damages the bacterial cell wall, allowing fluid to enter. The cell swells and finally bursts, releasing 100 to 200 phage particles.

10. How did Hershey and Chase "label" viral DNA and viral protein so that they could be distinguished?

Hershey and Chase used a radioactive isotope of sulfur to tag protein and a radioactive isotope of phosphorus to tag DNA. Because protein, but not DNA, contains sulfur, radioactive sulfur atoms were incorporated only into the protein of the phage. Similarly, the atoms of radioactive phosphorus labeled only the DNA, not the protein, because nearly all the phage's phosphorus is in its DNA.

11. Describe the means by which Hershey and Chase established that only the DNA of a phage enters an E. coli cell.

Hershey and Chase concluded that the DNA injected by the phage must be the molecule carrying the genetic information that makes the cells produce new viral DNA and proteins.

12. What are Chargaff's rules? How did he arrive at them?

Chargaff analyzed the base composition of DNA from a number of different organisms, whereby he noticed a peculiar regularity in the ratios of nucleotide bases. In the DNA of each species he studied, the number of adenines approximately equaled the number of thymines, and the number of guanines approximately equaled the number of cytosines. He developed the rules that [1] the base composition varies between species, and [2] within a species, the number of A and T bases are equal and the number of G and C bases are equal. The basis for these rules remained unexplained until the discovery of the double helix.

13. List the three components of a nucleotide.

A DNA nucleotide monomer consists of a nitrogenous base, the sugar deoxyribose, and a phosphate group.

14. Who built the first model of DNA and shared the 1962 Nobel Prize for discovery of its structure?

James Watson and Francis Crick

15. What was the role of Rosalind Franklin in the discovery of the double helix?

Franklin, a very accomplished X-ray crystallographer, conducted critical experiments resulting in the photograph that allowed Watson and Crick to deduce the double-helical structure of DNA.

16. Distinguish between the structure of pyrimidines and purines. Explain why adenine bonds only to thymine.

Adenine and guanine are purines, nitrogenous bases with two organic rings, while cytosine and thymine are nitrogenous bases called pyrimidines, which have a single ring. Thus, purines are about twice as wide as pyrimidines. A purine-purine pair is too wide and a pyrimidine-pyrimidine pair too narrow to account for the uniform 2-nm diameter of the double helix. Always pairing a purine (such as A) with a pyrimidine (such as T), however, results in a uniform diameter.

17. How did Watson and Crick's model explain the basis for Chargaff's rules?

Because each nitrogenous base is paired with its complement, the amount of A must equal the amount of T and the amount of G must equal the amount of C.

18. Given that the DNA of a certain fly species consists of 27.3% adenine and 22.5% guanine, use Chargaff's rules to deduce the percentages of thymine and cytosine.

The DNA of this fly species should consist of about 27.3% thymine and 22.5% cytosine.

19. Name the five nitrogenous bases.

Nitrogenous Base	*Purine or Pyrimidine*	*Where found*
adenine	purine	DNA, RNA
cytosine	pyrimidine	DNA, RNA
guanine	purine	DNA, RNA
thymine	pyrimidine	DNA
uracil	pyrimidine	RNA

20. Explain the base-pairing rule.

Adenine can form two hydrogen bonds with thymine and only thymine; guanine forms three hydrogen bonds with cytosine and only one cytosine.

21. Describe the structure of DNA.

The DNA molecule is 2 nm wide. The nucleotides are about 0.34 nm apart from each other. There are about 3.4 nm between each turn. The backbone consists of sugar and phosphate while the rungs are the nitrogenous base pairs.

22. Explain what is meant by 5' and 3'ends of the molecule.

The polynucleotide strand has directionality, from the 5' end (with the phosphate group) to the 3' end (with the –OH groups of the sugar). 5' and 3' refer to the numbers assigned to the carbons in the sugar ring. A strand is "read" from the 3' to the 5' end and "written" from the 5' to the 3' end.

23. What do we mean when we say the two strands of DNA are antiparallel?

The subunits of the two sugar-phosphate backbones run in opposite directions.

24. What is the semiconservative model of replication?

The semiconservative model predicts that when a double helix replicates, each of the two daughter molecules will have one old strand, from the parental molecule, and one newly made strand. This contrasts with the conservative model, in which the two parental strands somehow come back together (that is, the parental molecule is conserved). In the dispersive model, all four strands of DNA following replication have a mixture of old and new DNA.

25. Who performed the experiments that elucidated the correct mechanism of DNA replication?

Matthew Meselson and Franklin Stahl concluded that DNA replication is semiconservative.

26. How did Meselson and Stahl create "heavy" DNA for their experiments?

Meselson and Stahl cultured bacteria for several generations in a medium containing nucleotide precursors labeled with a heavy isotope of nitrogen, ^{15}N. They then transferred the bacteria to a medium with only ^{14}N, a lighter isotope. A sample was taken after DNA replicated once; another sample was taken after DNA replicated again. They extracted DNA from the bacteria in the samples and then centrifuged each DNA sample to separate DNA of different densities.

27. Explain how Meselson and Stahl confirmed the semiconservative mechanism of DNA replication.

The first replication in the ^{14}N medium produced a band of hybrid (^{15}N–^{14}N) DNA. This result eliminated the conservative model. The second replication produced both light and hybrid DNA, a result that refuted the dispersive model and supported the semiconservative model.

28. Define the origins of replication.

The replication of a DNA molecule begins at particular sites called origins of replication, short stretches of DNA having a specific sequence of nucleotides.

29–30. Distinguish between the leading and the lagging strands during DNA replication.

The DNA strand made by the mechanism of DNA replication forks is called the leading strand. Only one primer is required for DNA pol III to synthesize the leading strand. The DNA strand elongating *away from* the replication fork is called the lagging strand. In contrast to the leading strand, which elongates continuously in the 5' to 3' direction as the fork progresses, the lagging strand is synthesized discontinuously, as a series of segments.

Synthesis of the leading strand and synthesis of the lagging strand occur concurrently and at the same rate. The lagging strand is so named because its synthesis is delayed slightly relative to synthesis of the leading strand; each new fragment of the lagging strand cannot be started until enough template has been exposed at the replication fork.

31. What are Okazaki fragments? How are they welded together?

The series of segments of the lagging strand are called Okazaki fragments. The fragments are about 1,000 to 2,000 nucleotides long in *E. coli* and 100 to 200 nucleotides long in eukaryotes. Whereas only one primer is required on the leading strand, each Okazaki fragment on the lagging strand must be primed separately. After DNA pol III forms an Okazaki fragment, another DNA polymerase, DNA pol I, replaces the RNA nucleotides of the adjacent primer with DNA

nucleotides. But DNA pol I cannot join the final nucleotide of this replacement DNA segment to the first DNA nucleotide of the adjacent Okazaki fragment. Another enzyme, DNA ligase, accomplishes this task, joining the sugar-phosphate backbones of all the Okazaki fragments into a continuous DNA strand.

32. Identify the following enzymes.

helicase	untwists and separates strands
single stranded binding protein	holds DNA strands apart
primase	synthesizes RNA primer
DNA polymerase III	adds DNA nucleotides to new strand
topoisomerase	relieves strain caused by unwinding
DNA ligase	joins DNA fragments together
DNA polymerase I	removes RNA primer and replaces with DNA

34. Make a detailed list of the steps that occur in the synthesis of a new strand.

Helicase unwinds and separates the parental DNA strands. Topoisomerase breaks, swivels, and rejoins the parental DNA ahead of the replication fork, relieving the strain caused by unwinding. Molecules of single-strand binding protein stabilize the unwound parent strands. Primase synthesizes RNA primers, using the parental DNA as a template. The leading strand is synthesized continuously in the 5' to 3' direction by DNA polymerase III. Primase begins synthesis of the RNA primer for the lagging strand. DNA pol III discontinuously synthesizes the lagging strand in the 5' to 3' direction. DNA pol I removes all RNA primer sections and replaces them with DNA nucleotides. The replacement of the primer with DNA leaves the new DNA nucleotides with a free 3' end. DNA ligase joins the free 3' end to its adjacent 5' end, forming a continuous strand of DNA on both the leading and lagging strands.

35. Explain the roles of each of the following enzymes in DNA proofreading and repair.

Enzyme	*Role*
repair enzymes	detect and repair damaged DNA
nuclease	cuts damaged DNA strand; removes damaged sections
DNA polymerase	repair synthesis fills in missing nucleotides
ligase	seals free end of new DNA to old DNA, making strand complete

36. What is a thymine dimer? How might it occur? How is it repaired?

A thymine dimer is the covalent linking of thymine bases that are adjacent on a DNA strand. This causes the DNA to buckle and interferes with DNA replication. Teams of enzymes detect and repair damaged DNA.

38. Explain telomere erosion and the role of telomerase.

Eukaryotic chromosomal DNA molecules have special nucleotide sequences called telomeres at their ends. Telomeres do not contain genes; instead, the DNA typically consists of multiple repetitions of one short nucleotide sequence. Telomeric DNA acts as a kind of buffer zone that protects an organism's genes. In addition, specific proteins associated with telomeric DNA prevent the staggered ends of the daughter molecule from activating the cell's systems for monitoring DNA damage. Staggered ends of a DNA molecule, which often result from double-strand breaks, can trigger signal transduction pathways leading to cell cycle arrest or cell death.

39. Why are cancer cells immortal, but most body cells have a limited life span?

Normal shortening of telomeres may protect organisms from cancer by limiting the number of divisions that somatic cells can undergo. Cells from large tumors often have unusually short telomeres, as we would expect for cells that have undergone many cell divisions. Further shortening would presumably lead to self-destruction of the tumor cells. Researchers have found telomerase activity in cancerous somatic cells, suggesting that its ability to stabilize telomere length may allow these cancer cells to persist.