DNA

Section 12-1 pgs 286-294
DNA

- How do genes work?
- What are they made of, and how do they determine the characteristics of organisms?
- Are genes single molecules or are they longer structures made up of many molecules?
DNA

- In the middle of the 1900s, questions like these were on the minds of biologists everywhere.
- To truly understand genetics, biologists first had to discover the chemical nature of the gene.
DNA

- If the structures that carry genetic information could be identified, it might be possible to understand how genes control the inherited characteristics of living things.
Griffith and Transformation

- Like many stories in science, the discovery of the molecular nature of the gene began with an investigator who was actually looking for something else.
- In 1928, British scientist Frederick Griffith was trying to figure out how bacteria make people sick.
Griffith and Transformation

- More specifically, **Griffith wanted to learn how certain types of bacteria produce a serious lung disease known as pneumonia.**
- Griffith had isolated two slightly different strains, or types, of pneumonia bacteria from mice.
Griffith and Transformation

- Both strains grew very well in culture plates in his lab, but only one of the strains caused pneumonia.
- The disease-causing strain of bacteria grew into smooth colonies on culture plates, whereas the harmless strain produced colonies with rough edges.
Griffith and Transformation

- The differences in appearance made the two strains easy to distinguish.
- When Griffith injected mice with the disease-causing strain of bacteria, the mice developed pneumonia and died.
Griffith and Transformation

- When mice were injected with the harmless strain, they didn’t get sick at all.
- Griffith wondered if the disease-causing bacteria might produce a poison.
- To find out, he took a culture of these cells, heated the bacteria to kill them, and injected the heat-killed bacteria into the mice.
Griffith and Transformation

- The mice survived, suggesting that the cause of pneumonia was not a chemical poison released by the disease-causing bacteria.
- Griffith’s next experiment produced an amazing result.
Griffith and Transformation

- He mixed his heat-killed disease-causing bacteria with live, harmless ones and injected the mixture into mice.
- By themselves, neither should have made the mice sick.
Griffith and Transformation

- But to Griffith’s amazement, the mice developed pneumonia and many died.
- When he examined the lungs of the mice, he found them filled with not the harmless bacteria, but with the disease-causing bacteria.
Griffith and Transformation

- Somehow, the heat-killed bacteria had passed their disease-causing ability to the harmless strain.
- Griffith called this process \textit{transformation} because one strain of bacteria had apparently been changed permanently into another.
Griffith and Transformation

- Griffith hypothesized that when the live, harmless bacteria and the heat-killed bacteria were mixed, some factor was transferred from the heat-killed cells into the live cells.

- That factor, he hypothesized, must contain information that could change harmless bacteria into disease-causing ones.
Griffith and Transformation

- Furthermore, since the ability to cause disease was inherited by the transformed bacteria’s offspring, the transforming factor might be a gene.
Avery and DNA

- In 1944, a group of scientists led by Canadian biologist Oswald Avery at the Rockefeller Institute in New York decided to repeat Griffith’s work.
- They did so to determine which molecules in the heat-killed bacteria were most important for transformation.
Avery and DNA

- If transformation required just one particular molecule, that might well be the molecule of the gene.
- Avery and his colleagues made an extract, or juice, from the heat-killed bacteria.
Avery and DNA

- They then carefully treated the extract with enzymes that destroyed proteins, lipids, carbohydrates, and other molecules, including the nucleic acid RNA.
- Transformation still occurred.
Avery and DNA

- Obviously, since these molecules had been destroyed, they were not responsible for the transformation.
- Avery and the other scientists repeated the experiment, this time using enzymes that would break down DNA.
Avery and DNA

- When they destroyed the nucleic acid DNA in the extract, transformation did not occur.
- There was just one possible conclusion.
- DNA was the transforming factor.
Avery and DNA

- Avery and the other scientists discovered that the nucleic acid DNA stores and transmits the genetic information from one generation of an organism to the next.
The Hershey-Chase Experiment

- Scientists are a skeptical group.
- It usually takes several experiments to convince them of something as important as the chemical nature of the gene.
The Hershey-Chase Experiment

- The most important of these experiments was performed in 1952 by two American scientists, Alfred Hershey and Martha Chase.
- They collaborated in studying viruses, nonliving particles smaller than a cell that can infect living organisms.
The Hershey-Chase Experiment

● One kind of virus that infects bacteria is known as a bacteriophage, which means “bacteria eater”.

● Bacteriophages are composed of a DNA or RNA core and a protein coat.
The Hershey-Chase Experiment

- When a bacteriophage enters a bacterium, the virus attaches to the surface of the cell and injects its genetic information into it.

- The viral genes act to produce many new bacteriophages, and they gradually destroy the bacterium.
The Hershey-Chase Experiment

● When the cell splits open, hundreds of new viruses burst out.

● Hershey and Chase reasoned that if they could determine which part of the virus—the protein coat or the DNA core—entered the infected cell, they would learn whether genes were made of protein or DNA.
The Hershey-Chase Experiment

● To do this, they grew viruses in cultures containing radioactive isotopes of phosphorus-32 ($^{32}$P) and sulfur-35 ($^{35}$S).

● This was a clever strategy because proteins contain almost no phosphorus and DNA contains no sulfur.
The Hershey-Chase Experiment

- The radioactive substances could be used as markers.
- If $^3{}^{35}\text{S}$ was found in the bacteria, it would mean that the viruses’ protein had been injected into the bacteria.
- If $^3{}^{32}\text{P}$ was found, the DNA was injected.
The Hershey-Chase Experiment

- The two scientists mixed the marked viruses with bacteria.
- Then, they waited a few minutes for the viruses to inject their genetic material.
- Next, they separated the viruses from the bacteria and tested the bacteria for radioactivity.
The Hershey-Chase Experiment

- Nearly all the radioactivity in the bacteria was from phosphorus, the marker found in DNA.
- Hershey and Chase concluded that the genetic material of the bacteriophage was DNA, not protein.
The Components and Structure of DNA

- You might think that knowing genes were made of DNA would have satisfied scientists, but that was not the case at all.
- Instead, they wondered how DNA, or any molecule for that matter, could do three critical things that genes were known to do.
The Components and Structure of DNA

- First, genes had to carry information from one generation to the next.
- Second, they had to put that information to work by determining the heritable characteristics of organisms.
The Components and Structure of DNA

- Third, genes had to be easily copied because all of a cell’s genetic information is replicated every time a cell divides.
- For DNA to do all of that, it would have to be a very special molecule indeed.
The Components and Structure of DNA

- DNA is a long molecule made up of units called nucleotides.
- Each nucleotide is made up of three basic components: a 5-carbon sugar called deoxyribose, a phosphate group, and a nitrogenous base.
The Components and Structure of DNA

- There are four kinds of nitrogenous bases in DNA.
- Two of the nitrogenous bases, adenine and guanine, belong to a group of compounds known as purines.
The Components and Structure of DNA

- The remaining two bases, cytosine and thymine, are known as pyrimidines.
- Purines have two rings in their structures, whereas pyrimidines have one ring.
The Components and Structure of DNA

- The **backbone of a DNA chain is formed by sugar and phosphate groups** of each nucleotide.
- The nitrogenous bases stick out sideways from the chain.
- The nucleotides can be joined together in any order, meaning that any sequence of bases is possible.
The Components and Structure of DNA

- In the 1940s and early 1950s, the leading biologists in the world thought of DNA as little more than a string of nucleotides.
- The four different nucleotides, like the 26 letters of the alphabet, could be strung together in many different ways, so it was possible that they could carry coded genetic information.
The Components and Structure of DNA

- However, so could many other molecules, at least in principle.
- Was there something more to the structure of DNA?
The Components and Structure of DNA

- One of the puzzling facts about DNA was a curious relationship between its nucleotides.
- Years earlier, Edwin Chargaff, an American biochemist, had discovered that the percentages of guanine [G] and cytosine [C] bases are almost equal in any sample of DNA.
The Components and Structure of DNA

- The same thing is true for the other two nucleotides, adenine [A] and thymine [T].
- The observation that \([A] = [T]\) and \([G] = [C]\) became known as Chargaff’s rules.
The Components and Structure of DNA

- Despite the fact that the different DNA samples from organisms as different as bacteria and humans obeyed this rule, neither Chargaff nor anyone else had the faintest idea why.
- In the early 1950s, a British scientist named Rosalind Franklin began to study DNA.
The Components and Structure of DNA

- She used a technique called X-ray diffraction to get information about the structure of the DNA molecule.
- Aiming a powerful X-ray beam at concentrated DNA samples, she recorded the scattering pattern of the X-rays on film.
The Components and Structure of DNA

- Franklin worked hard to make better and better patterns from DNA until the patterns became clear.
- By itself, Franklin’s X-ray pattern does not reveal the structure of DNA, but it does carry some very important clues.
The Components and Structure of DNA

- The X-shaped pattern that was shown revealed that the strands in DNA are twisted around each other like the coils of a spring, a shape known as a helix.
- The angle of the X suggests that there are two strands in the structure.
The Components and Structure of DNA

- Other clues suggest that the nitrogenous bases are near the center of the molecule.
- At the same time that Franklin was continuing her research, Francis Crick, a British physicist, and James Watson, an American biologist, were trying to understand the structure of DNA by building three-dimensional models of the molecule.
The Components and Structure of DNA

- Their models were made of cardboard and wire.
- They twisted and stretched the models in various ways, but their best efforts did nothing to explain DNA’s properties.
The Components and Structure of DNA

- Then, early in 1953, Watson was shown a copy of Franklin’s remarkable X-ray pattern.
- The effect was immediate.
- In his book *The Double Helix*, Watson wrote: “The instant I saw the picture, my mouth fell open and my pulse began to race.”
The Components and Structure of DNA

- Using clues from Franklin’s pattern, within weeks Watson and Crick had built a structural model that explained the puzzle of how DNA could carry information, and how it could be copied.
- They published their results in a historic one-page paper in April of 1953.
The Components and Structure of DNA

- Watson and Crick’s model of DNA was a double helix, in which two strands were wound around each other.
- A double helix looks like a twisted ladder or a spiral staircase.
The Components and Structure of DNA

- When Watson and Crick evaluated their DNA model, they realized that the double helix accounted for many of the features in Franklin’s X-ray pattern, but did not explain what forces held the two strands together.
The Components and Structure of DNA

- They then discovered that hydrogen bonds could form between certain nitrogenous bases and provide just enough force to hold the two strands together.
- Hydrogen bonds can form only between certain base pairs—adenine and thymine, and guanine and cytosine.
The Components and Structure of DNA

- Once they saw this, they realized that this principle, called base-pairing, explained Chargaff’s rules.
- Now there was a reason $[A] = [T]$ and $[G] = [C]$. 
The Components and Structure of DNA

- For every adenine in a double-stranded DNA molecule, there had to be exactly one thymine molecule; for each cytosine molecule, there was one guanine molecule.