Chapter 16 - The Molecular Basis of Inheritance

Determining the Chemical Composition of DNA

* After \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ determined that genes were on chromosomes, scientists began wondering what they were made of.
* Early on, scientists thought they were made of \_\_\_\_\_\_\_\_\_\_\_\_ because they were large and structurally sound.
* \_\_\_\_\_\_\_\_\_\_\_ were deemed too simple to carry out the complex tasks chromosomes required.
* As scientists continued their experiments with viruses and bacteria, many results were observed that gave support to the notion that DNA was the \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* A classic experiment demonstrated the \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_role of DNA.

Frederick Griffith

* Studied the bacterium that caused pneumonia.
* Worked with two strains: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ and \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* An experimental overview:
* (S) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ cells produce mucous capsules that protect the bacteria from an organism’s immune system--\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* (R) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ cells have no mucous capsule and are attacked by an organism’s immune system--\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

Frederick Griffith, His Experiment

* Mixed \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ pathogenic (S) bacteria with \_\_\_\_\_\_\_\_\_\_\_\_\_ non-pathogenic (R) bacteria, the non-pathogenic (R) bacteria began producing the mucous capsule and became \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (S).
* The new bacteria that arose from the bacteria were somehow \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ into pathogenic S. pneumonia.
* Griffith called this process \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

Griffith’s Transformation Experiment

* Did \_\_\_\_\_\_ identify DNA as the transforming factor, but it set the stage for other experiments.

Oswaldt Avery

* Avery worked for a long time trying to \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ the transforming factor.
* After isolating and purifying numerous \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ from the heat killed pathogenic bacteria he and his colleagues could only get DNA to work.
* The prevailing beliefs about proteins vs. DNA continued to generate skepticism.

The Hershey-Chase Experiment

* In 1952, Alfred Hershey and Martha Chase performed experiments with \_\_\_\_\_\_\_\_\_\_\_\_ showing that DNA is genetic material.
* Viruses (aka phages) are \_\_\_\_\_\_\_ or \_\_\_\_\_\_\_\_ wrapped in a protein.
* \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ is a bacteria that is often used in experiments.
* Used the \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ because it was generally accepted to be DNA wrapped in protein.
* Used E. coli because it was easily obtainable and was readily attacked by T2.
* Had to demonstrate whether it was \_\_\_\_\_\_\_ or \_\_\_\_\_\_\_\_\_\_\_\_\_\_ that was the hereditary factor.
* Their experiment demonstrated which part of the T2 entered the E. coli.
* They grew T2 in the presence of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_--proteins contain sulfur, DNA does not.
* Next, they grew the T2 in a separate batch of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. The DNA of T2 contains phosphorous--the proteins do not.
* The scientists now had 2 batches of T2, one labeled with radioactive sulfur and one labeled with radioactive phosphorous.
* These 2 batches were \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ with non-radioactive samples of E. coli and analyzed shortly after infection.
* Shortly after infection, the E. coli samples were spun in a blender to \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ loose parts of T2.
* The mixtures were then spun in high speed \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ for a long time to separate out various parts of the mixture.
* At the bottom of the tube was a \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* The pellet was examined for radioactivity and radioactive \_\_\_\_\_\_\_\_\_\_\_\_\_\_ was found.
* The \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ was analyzed and a lot of radioactive sulfur was found, but no radioactive phosphorous.
* This indicates that the \_\_\_\_\_\_\_ got into the E. coli and was in the pellet
* The \_\_\_\_\_\_\_\_\_\_\_\_\_ did not get into the bacteria and was left in the supernatant.
* Furthermore, when the bacteria in the pellet were \_\_\_\_\_\_\_\_\_\_\_ on culture medium, they produced more T2 containing radioactive phosphorous.
* They concluded:
	+ That the \_\_\_\_\_\_\_\_\_\_ injects \_\_\_\_\_\_\_ into the E. coli and it is the genetic material that programs the cells to produce new T2 phages.
	+ The protein stays \_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* This experiment provided firm evidence that DNA was the \_\_\_\_\_\_\_\_\_\_material and not protein.

Erwin Chargaff’s Experiment

* It provided \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ that DNA was the genetic material.
* He \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ the notion that DNA was not complex enough to comprise hereditary material. Chargaff showed the diversity of the DNA molecule and that its composition \_\_\_\_\_\_\_\_\_\_\_\_\_from organism to organism.
* He discovered that the amount of \_\_\_\_\_\_\_\_\_\_\_\_\_\_ is equal to the amount of \_\_\_\_\_\_\_\_\_\_\_\_\_ and \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ equaled the amount of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* Chargaff did not know what all of this meant, but after the elucidation of the shape of the DNA molecule, these became known as \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.

Watson and Crick

* In 1953, James Watson and Francis Crick visited a lab of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* Examined an X-ray diffraction image of DNA produced by \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* Their familiarity with such diffraction patterns allowed them to quickly deduce that DNA consisted of \_\_\_\_strands and was \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_in shape.
* Through trial and error they concluded \_\_\_ paired with \_\_\_ and \_\_\_ with \_\_\_. This gave the uniform width they determined from the work of Franklin and explained Chargaff’s findings.
* They explained the base paring rules, the shape and the width of the DNA and showed that none of this was dependent on the \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_of the nucleotides.
* Thus, the DNA could be put together an \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ number of ways.
* The question now arose for how DNA was \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* The strands are said to be \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ to each other.
* That is, they contain the information necessary to \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ each other.
* But how?
* These men proposed a \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ model in which the new DNA strand formed contained 1/2 of the original DNA and 1/2 newly synthesized DNA--one strand was original and one strand was new.
* They \_\_\_\_\_\_\_\_\_\_\_\_rule out a model where somehow the old DNA stayed together and the newly synthesized DNA strand was completely new.
* Additionally, they could not rule out a \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ model where both strands of DNA consisted of old and new DNA.
* The mechanisms for these three models were difficult to elucidate but Matthew \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ and Franklin \_\_\_\_\_\_\_\_\_\_\_\_\_\_ developed experiments to test them.

The Meselson-Stahl Experiment

* E. coli cells were cultured in a medium containing \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, 15N.
* After several generations the bacteria were transferred into a medium containing \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, 14N.
* Ideally, all DNA synthesized the \_\_\_\_\_\_\_\_\_\_ time through contained heavy nitrogen.
* All DNA synthesized in the normal nitrogen tube (after the transfer) would be \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ than the DNA from the original culture.
* Their hypotheses: (what would be seen after centrifuging the tubes containing DNA)
	+ If replication followed the \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ model, the first replication would contain 2 bands of DNA, one \_\_\_\_\_\_\_ and one \_\_\_\_\_\_\_\_\_; and the 2nd replication would show the \_\_\_\_\_\_ thing (2 bands).
* Their hypotheses: (what would be seen after centrifuging the tubes containing DNA)
	+ If it followed the \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ model, one band would be seen containing \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ DNA. This was seen after the first replication, but \_\_\_\_\_ the second\*.
* Their hypotheses: (what would be seen after centrifuging the tubes containing DNA)
	+ If it followed the \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ model \_\_\_\_ band would be seen after the first replication and \_\_\_ would be seen after the 2nd replication.
* After they transferred the DNA from the 15N tube to the 14N tube, they waited 20 minutes (\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_) and then centrifuged the tube.
* They were able to detect \_\_\_\_\_ band in the centrifuge tube.
* In a separate tube, they waited for \_\_ rounds of replication (40 min.) and were able to detect \_\_ bands in the centrifuge tube.
* Conclusion:
	+ The \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ model was followed. A \_\_\_\_\_\_\_\_\_ band was detected following the 1st replication and 2 bands, (one \_\_\_\_\_\_ and one \_\_\_\_\_\_\_\_\_) were detected following the 2nd replication.

DNA Replication

* Begins at a site called the \_\_\_\_\_\_\_\_\_ of replication.
* Prokaryotes have \_\_\_ origin of replication.
* Eukaryotes have \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ of origins of replication.
* \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ are the short nucleotide fragments (DNA or RNA) with an available free 3’ end to which DNA polymerase III (DNA pol III) will \_\_\_\_\_ nucleotides according to the base paring rules.
* \_\_\_\_\_\_\_\_\_\_\_\_\_\_ is the enzyme that starts an RNA chain from scratch creating a primer that can initiate the synthesis of a new DNA strand.
* The \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ strand of DNA synthesis only needs \_\_\_ primer.
* The \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ strand needs a new primer for each \_\_\_\_\_\_\_\_\_\_\_\_\_ fragment added to the growing strand.
* \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ are enzymes that catalyze the elongation of DNA at the replication fork.
* One by one, \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ are added by DNA polymerase to the growing end of the DNA strand--the free 3’ end.
* DNA \_\_\_\_\_\_\_\_\_\_\_ grows \_\_\_-->\_\_\_ adding to the free 3’ end.
* The 2 strands of the DNA are \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, they are oriented in opposite directions.
* This poses replication problems.
* DNA polymerase only adds nucleotides to the \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_. Thus, it can only elongate in the 5’-->3’ direction.
* You get what is known as a \_\_\_\_\_\_\_\_\_\_\_\_\_\_ strand and a \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ strand.

DNA Replication

* As we said earlier, primase works to join RNA nucleotides together creating primers \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_to the DNA template strand.
* This is the site of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_, and new DNA strands will be synthesized here.
* When cellular DNA is replicated, the \_\_\_\_\_\_\_\_\_\_\_\_ is a short stretch of RNA with a free 3’ end.
* DNA \_\_\_\_\_\_\_\_\_\_\_\_ functions to replace the RNA nucleotide primers with DNA.
* All of the nucleotides of the RNA primer are replaced by DNA pol I.
* DNA \_\_\_\_\_\_\_\_\_ joins the gap left between the last two nucleotides joining all of the Okazaki fragments into \_\_\_ continuous strand.
* \_\_\_\_\_\_\_\_\_\_\_\_\_ is the enzyme responsible for \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ the double helix at the replication fork.
* This \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ the parental strands of DNA making them available for use as template strands.
* This untwisting actually causes a greater amount of twisting ahead of the replication fork, and an enzyme called \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ helps to reduce this twisting.
* After helicase separates the two parental strands, single strand binding protein binds to the DNA strands \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ them until new DNA synthesis occurs.
* Keep in mind that all of the molecules described in the replication process actually work together to \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ DNA production.
* Think of them as the individual parts of a “\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.”
* The main importance of replicating the DNA is the ability to do it \_\_\_\_\_\_\_\_\_\_\_\_\_\_ error.
* Errors in completed eukaryotic DNA occur in approximately \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ nucleotides.
* Initial errors occur at a rate of about 1 in 100,000. Proofreading mechanisms by \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ fix many of the problems.
* If an error escapes proofreading, they are often fixed by special enzymes within the cell--but even these are not \_\_\_\_\_\_\_\_ effective at removing all errors.
* Additionally, some errors occur \_\_\_\_\_\_\_ DNA synthesis has been completed.

Excision Repair

* Errors that occur as a result of the \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (radiation, chemicals, X-rays, etc.) can often be fixed by DNA \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ & \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* This is a way the cell tries (usually effectively) to \_\_\_\_ problems before they get perpetuated (cancer).

Telomeres

* When we get to the end of the chromosome, we encounter what are known as telomeres, and they create a problem for \_\_\_\_\_\_\_\_\_\_\_ DNA.
* At the end of the lagging strand, when the RNA primer is removed, there is no free 3’ end to which nucleotides can be added.
* Telomeres consist of \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ repetitions of one short nucleotide sequence.
* This helps \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ the DNA from multiple rounds of DNA synthesis and \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ the erosion of genes near the end of the DNA molecule.
* Thus, \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ rounds of DNA synthesis would result in shorter and shorter DNA molecules.
* This is okay in \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ cells where cell division is somewhat limited.
* In \_\_\_\_\_\_\_\_\_\_\_\_\_\_, however, it is necessary to preserve the genetic complement.
* Cells do this using an enzyme called \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_.
* This enzyme \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ the length of the germ cell telomeres thus preserving the amount of DNA.

Telomerases

* Telomerases act to \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ the DNA of human gametes which would become progressively shorter during successive rounds of DNA synthesis.
* Eventually, the germ cells’ telomeres would become so short that the genes would become \_\_\_\_\_\_\_\_\_\_\_\_\_\_ and the cell would begin to \_\_\_\_\_\_\_\_ genes.