L.6 Molecular Genetics

Is the area of genetics concerned with the reinterpretation of Mendlian genetics in molecular terms .Its deal with the genetic materials , deoxyribonucleic acid (DNA),the replication of DNA produce more DNA, there transcription of DNA into ribonucleic acid (RNA) and the translation of RNA into protein.

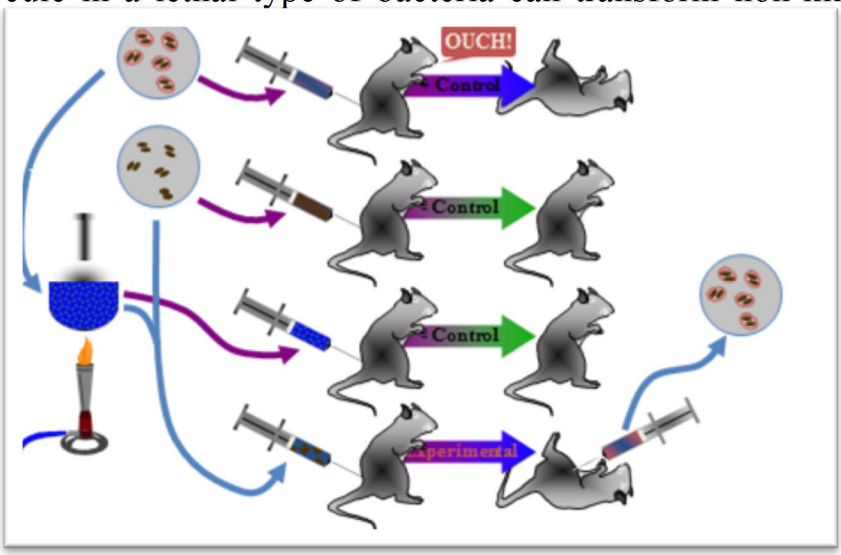
Experiments identify and describe the genetic material:

Many different experiments demonstrate that DNA contains the instructions for producing the heritable traits of all single –celled and multicelled organisms .One of these experiments:

Experiments identify and describe the genetic material:

Griffth reported that heat killed bacteria of one type could transform living bacteria of a different type .He demonstrated this transformation by using 2 strains of bacterium *streptococcus pneumonia*, one strain (s) produced smooth colonies (cell had polysaccharide capsules),it caused bacterial infection in mice .Another strain (R) which lacked polysaccharide capsules produced rough colonies.

Griffth found that neither heat killed (S-type) nor live (R-type) cells by themselves, caused pathogen in mice. However, if a mixture of live R type and heat killed S-type cells was injected into mice ,the mice developed a bacterium identical to that caused by injection of living S type cells thus something's in the things in the heat –killed S-type cells transformed the R-type bacteria into S-type cells. This experiment showed that molecule in a lethal type of bacteria can transform non-killing bacteria into killer .

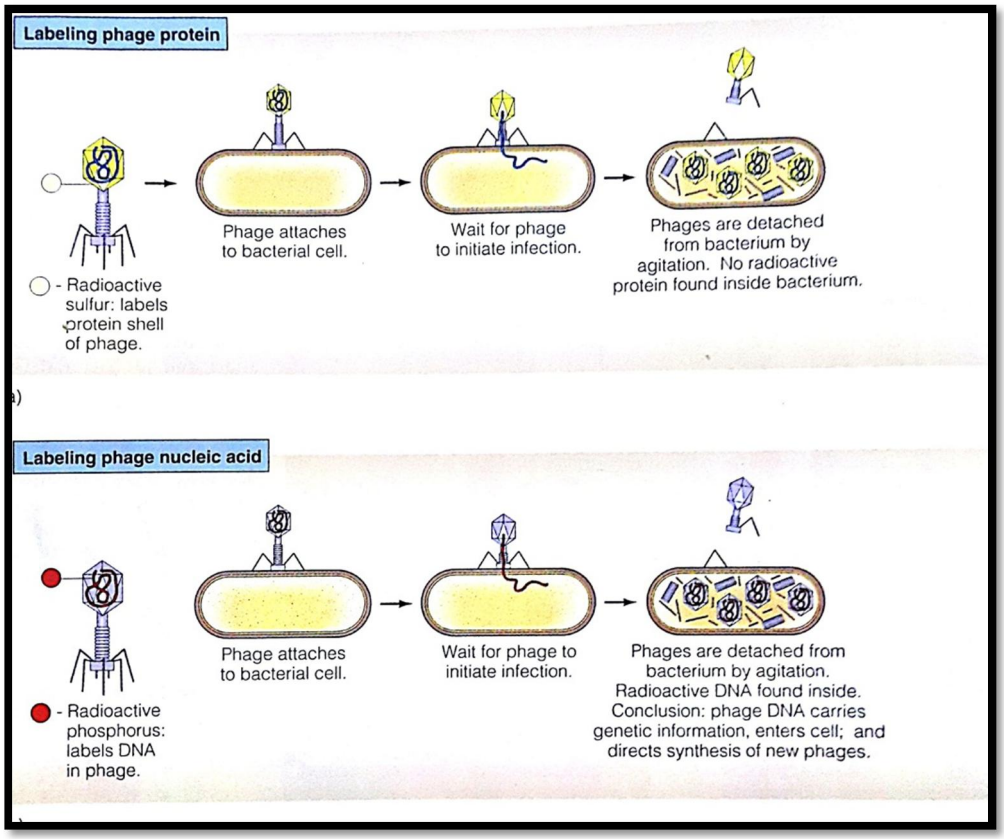


This experiment do not show and demonstrate the DNA is a genetic material, therefore the U.S. physician Avery, Macleod and Mccarthy investigated the chemical nature of this transforming factor .

First, they lysed heat-killed S cells extracted from *Streptococcus pneumonia*. When the lysate combined with R bacteria, virulent S bacteria were produced.

To determine the factor responsible for transformation, Avery, MacLeod, and McCarty removed the sugar coats, proteins, RNA, and DNA from the lysate. The R bacteria remained nonvirulent only when the DNA was removed from the lysate. In all other cases, the R bacteria were transformed. This experiment showed that DNA was the "transforming principle."

Hershey and Chase used different radioactive molecules to distinguish the viral protein coat from the genetic material (DNA).These experiments showed that the virus transfers DNA and not protein, to the bacterium. Therefore, DNA is the genetic material .This experiment used particular types of sulfur and phosphorus atoms that emit detectable radiation .



DNA structure:

DNA is large macromolecules (polymers) with three types of components:

1-Sugar:

A five carbon sugar (pentose) in DNA , the sugar is deoxyribose .

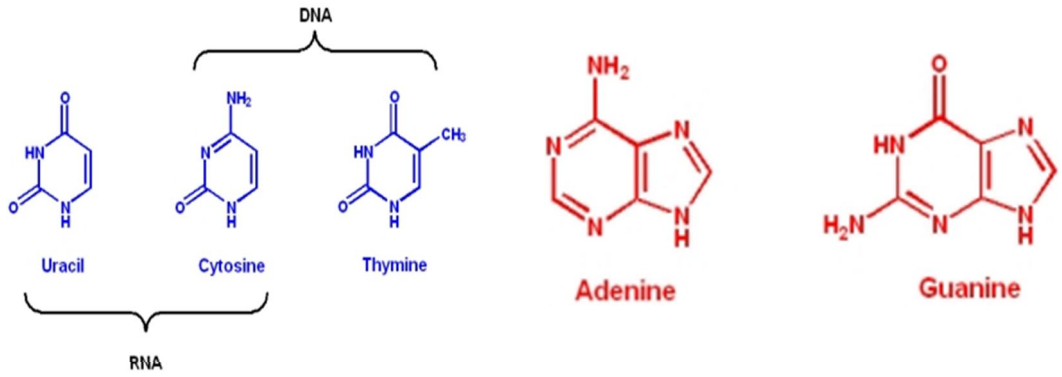
2- Phosphate

3- Base:

Is nitrogen containing base. It may be purine (A,G) or pyrmidine (C,T) . One base, one sugar and one phosphate combine to form a nucleotide . Nucleotides combine to form poly nucleotides (figure 3.).

A nucleoside: Is composed of base and sugar.

DNA proposed by the Watson and Crick in 1953



Pyrimidines **Purines**

Watson and Crick model of DNA :

The major features of that model as the following:

1. DNA is a double stranded molecule consists of 2 polynucleotide chains running in opposite directions. Those are arranged into a ladder-like structure twisted to form a double helix.
2. The bases are on the inside of the molecules and the 2 chains are joined together by double H-bond between A and T and triple H-bond between C and G.
3. The total amount of purines(A+G) equals the total amount of pyrmidines

4. The base pairing is very specific which make the 2 strands complementary to each other.
5. The individual nucleotides in each strand are linked covalently between the phosphate group of one nucleotide and deoxyribose sugar of the next nucleotide.
6. These linked sugars and phosphates form the outer back bones of the double strand DNA, the bases are oriented in ward, forming the molecules core.
7. So each strand contains all the required information for synthesis (replication) of a new copy to its complementary.

Types of DNA:

There are three alternative forms of DNA :

1-B-form helix:

It is the most common form of DNA in cells characterized by:

1. Right-handed helix
2. Contain 2 grooves;
   a- Major groove (wide): provide easy access to bases
   b- Minor groove (narrow): provide poor access.

2-A-form DNA:

It's less common form of DNA characterized by:

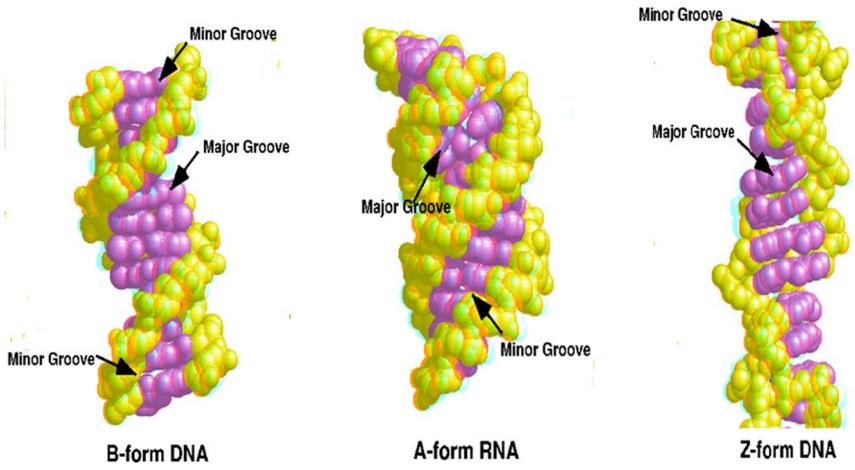
1. Right handed helix
2. Contain 2 different grooves:
   a- Major groove: very deep and narrow
   b- Minor groove: very shallow and wide (binding site for RNA)

3- Z-form DNA:

It’s a radical change of B-form :

1. Left handed helix, very extended
2. It is GC rich DNA regions.
3. The sugar base backbone form Zig-Zag shape

4. The B to Z transition of DNA molecule may play a role in gene regulation.



Replication of DNA (Semiconservative)

Watson and Crick suggested a simple mechanism for this replication called semiconservative. Some researchers suggested that DNA might replicate in any of three possible ways: Semiconservative, conservative or dispersive

Conservative: One double helix specifying creation of a second double helix

Dispersive: Double helix cutting into pieces that would join with newly synthesized DNA pieces to form 2 molecules.

Semiconservative replication:

Replication begins at specific sites on the double helix, called origins of replication, in which the two chains are separate from each other when a helicase enzyme breaks the hydrogen bonds that connect a base pair, helicase can also repair errors in replicated DNA. A site where DNA is locally opened, resembling a fork , is called a replication fork**.** Binding proteins hold the two strands apart .Another enzyme primase makes a short stretch of RNA on the DNA template called RNA primer. The RNA primer was required because the major replication enzyme **DNA polymerase** can only add bases to RNA primer. Next, the RNA primer attracts DNA polymerase, which brings in DNA nucleotides complementary to the exposed bases on the parental strand; this strand serves as a template. New bases are added one at a time, starting at

the RNA primer. The new DNA strand grows as hydrogen bonds form between the complementary bases

DNA polymerase works directionally, adding new nucleotides to the 3'end of sugar in the growing strand. Overall, replication proceeds in 5' to 3' direction. That called continuous strand (leading strand). The replication of the other strand is discontinuous (or lagging strand) by forming small pieces of DNA , these pieces up to 150 nucleotides are called Okazaki fragments on the 5' to 3' template. When an Okazaki fragment forms, DNA polymerase I removes the RNA primer and replaces it with DNA adjacent to the fragment. Ligase is an enzyme that seals sugar –phosphate back bones of the pieces building the new strand.

DNA polymerase also proofreading activity checks and replaces incorrect bases, as well as removes RNA primer from the semiconservative replication from two double helices each of which containing original strand.