Chpt 8 and Beyond: DNA/RNA History, Structure and Replication

Biology History

1670's **discovery of microscopic life**
Leeuwenhoek

1730's **classification of life**: plants & anim
Linnaeus

1830's - 1850's **Cell Theory**
-taxonomy now includes microorgan
-cells come from pre-existing cells

1860's -Darwin explains the relatedness of all life through **Evolution by Natural Selection**
-**chemical make-up of cell nucleus** is found to be 1/2 protein, 1/2 something else unknown

1880's biologists saw **chromosomes** in dividing cells

1890's unknown substance in nucleus is identified and called **DNA**

1902 Walter Sutton proposed that hereditary material is located on chromosomes
Chromosomal Theory of Heredity

1910 Thomas Hunt Morgan discovered **genes located** on chromosomes supporting Sutton's proposal

But **chemically, chromosomes are 1/2 protein &1/2 DNA**
what do you know that makes this statement true?

So the big question was: **are genes made of protein or DNA?**
from the 1920's on scientists tried to answer this question

1928 Frederick Griffith, British bacteriologist, experimented w/strain S & strain R bacteria: strain S w/mucous coat caused pneumonia, strain R w/out mucous coat did not cause pneum

Griffith was actually trying to develop a vaccine for pneumonia, but he stumbled onto something interesting

Griffith mixed dead strain S w/live strain R bacteria, injected this into mice & they got pneumonia and died

he concluded that something passed from strain S to R to change R into the lethal form

he called this a transforming factor

transformation: process where bacteria are changed by absorbing genetic material from an outside source

Did this experiment answer the big question? is protein or DNA the genetic material?

1944 American bacteriologists **Avery,MacLeod, & McCarty** produced strong evidence that DNA was the transforming factor

- they took molecules from heat killed S strain & used enzymes to destroy proteins, lipids, carbs, & RNA but strain R was still transformed to strain S
- then they used enzymes to destroy DNA and no transformation occurred
- they concluded that DNA was the transforming factor, **DNA is the genetic material**

but science always needs lots of more evidence

many scientists did many experiments to further support these findings and all evidence was leading to the same conclusion, so some moved on to the structure of DNA

Last famous experiment was the **Hershey & Chase** experiment in **1952**
- they used radioactive S & radioactive P to trace proteins & DNA
- S is in proteins, but not DNA, P is in DNA, but not proteins
- they also used bacteriophage viruses
  - these are viruses that attack and infect bacteria
- so what is a **virus**? a borderline form of life
  - -they are not cellular
    - no cell membrane, no cellular organelles, no cytoplasm, no nucleus
  - -but they do have DNA, an outer protein coat, a few enzymes and they can reproduce themselves BUT ONLY by using a living host
- remember bacteria, the simplest forms of life, prokaryotes, also have no nucleus, but they do have DNA, a cell membrane, cytoplasm, ribosomes, they have no mitochondria nor chloroplasts, but they do have a cellular pathway that allows them to make energy by the process of CR and some of them can photosynthesize because they have chlorophyll and they can reproduce themselves, in fact, bacteria have a very rapid life cycle, reproducing as often as every 20 minutes

viruses have no ability of their own to make E, so they must harness and use a living host

- so, back to the experiment
  - one batch of virus was labeled with radioactive P, another batch was labeled with radioactive S
- they allowed viruses to attack the bacteria & inject their reproductive info inside
- then they centrifuged the bacteria & virus
  - this separates substances, heavier particles settle out of solution, so live bacteria would be at bottom, virus coat would be in liquid
- the batch w/radioactive protein was only in liquid, the batch w/radioactive DNA was only in solids (inside bacteria)
- thus **DNA was genetic material** not protein and this experiment **definitively** answered the question

So in 1952, DNA was finally accepted to be genetic material

However with mounting evidence from 1944-1952, many scientists had already decided it was DNA and the next big question was: **What is the structure of DNA?** many scientists were racing to find out

1950 American biochemist **Erwin Chargaff** analyzed 4 N bases found in DNA

he examined DNA in many many different species

he **found 2 things**

1- the amount of the bases varies from species to species

humans 30.3% is base A

E. coli 26% A

2- the amount of A = amount of T

amount of C = amount of G

these are known as called **Chargaff's Rules**

1950 Rosalind Franklin & Maurice Wilkins photographed DNA w/X-ray crystallography technique where X-rays are passed through a crystalline structure & forms picture on photographic film

Rosalind had photographed many substances could tell 3D shape of molecule from picture

her **picture of DNA gave 3 pieces of info**

1- showed X shape------->helix

2- could measure actual width of molecule

3- picture showed molecule had an equal width along the whole length

American **James Watson** received his BS in Zoology (Ornithology) at Chicago University 1950 received his PhD from Indiana University at age 23
from there he studied bacteriophage viruses in Copenhagen, then moved to Cambridge where he met Francis Crick and began studying with him (1950)
Francis Crick was originally a physicist, now was studying biology
Watson convinced Francis to work on the structure of DNA, Watson wanted to be famous for this
the two of them saw Rosalind Franklin's picture of DNA which was crucial to figuring out the structure

1953 James Watson & Francis Crick figured out and **published structure of DNA**
they figured it out from looking at data & work of many different scientists, put it all together by playing with models

from Rosalind's picture, they knew it was a helix, but was it single or double-stranded?
they knew DNA was made of deoxyribose sugar, 4 different N bases, & phosphate
the width was too large to be single-stranded
P - sugar - N base
the width was also uniform
now they had to examine the bases

from chemical info of 4 N bases: they knew
adenine & guanine are larger bases and have 2 rings (purines) in structure
cytosine & thymine are smaller and have 1 ring (pyrimidines)

-if 2 like bases pair together: A-G, C-T
the structure would not have uniform width
so how can bases pair up?

from Chargaff's Rules: amounts A=T and the amounts C=G
so they then looked at structure noting that A could easily make 2 hydrogen bonds w/T and G could easily make 3 H bonds w/C,
therefore, A must pair with T and C must pair with G

Thus, **DNA** molecule consists of long strands of
- nucleotides joined together
- phosphate - sugar make up backbone of ladder
- nitrogen bases make up rungs of ladder
  - 2 are purines, 2 rings: A & G
  - 2 are pyrimidines, 1 ring: C & T
- **N bases held together by H bonds**
- **2 strands are complementary**
  - knowing struct of 1 side tells struct of other
- strands are **antiparallel**
  - 3'------->5' direction on one strand
  - 5'------->3' direction on other strand

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