Chpt 16: The Molecular Basis of Inheritance

DNA/RNA History, Structure, 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 chemical make-up of cell nucleus is found to be 1/2 protein, 1/2 something else unknown
-Darwin explains the relatedness of all life through Evolution by Natural Selection

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
supported Sutton's proposal

But chemically, chromosomes are 1/2 prot 1/2 DNA

So the big question was: are genes made of protein or DNA?

1920's on scientists tried to answer this quest

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 on 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 Griffith's exp answer big question? is prot or DNA the genetic material? No

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 except ribosomes, no nucleus, no cytoplasm
  - but do have DNA, an outer protein coat, and they can reproduce themselves if they use a living host

- so, 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

4 N bases: adenine & guanine are larger bases
have 2 rings (purines), cytosine & thymine
are smaller 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?
then looked at structure noting that A could
easily make 2 hydrogen bonds w/T
G could easily make 3 H bonds w/C
then looked at Chargaff's Rules, amts A=T,
amts C=G, therefore this is how they must
bond

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