

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 saw Rosalind Franklin's picture of DNA, met Francis Crick, originally a physicist, now studying biology
and the two decided to figure out the structure of DNA (1951)

Watson did want to be famous for this

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

1952 Am geneticists Martha Chase & Alfred Hershey definitively answered the question worked w/bacteriophage viruses: viruses that attack & destroy bacteria

life cycle of phage virus: attaches to outside of bacteria, injects info inside, info takes over bacterial cell, makes copies of virus, rupture cell

since injected material takes over cell, it must be hereditary material

viruses made of only 2 things: DNA & protein