

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, no cytoplasm, no nucleus
-but they do have DNA, an outer protein coat, a few enzymes and they can reproduce themselves if they use 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
viruses have no ability of their own to make E, so they must harness 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

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