DNA : The Genetic Material

* After Mendel, scientists knew that some kind of genetic material was located on chromosomes. They did not know which macromolecule (DNA or protein) was the source of this genetic information

Fredrick Griffith → discovering transferring substance

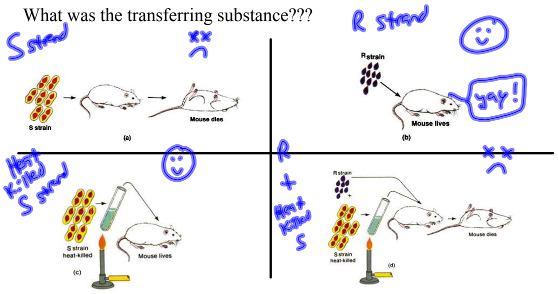
- studied two strains of pneumonia (mice)
  - a smooth strand (S) and a rough (R) strand

caused pneumonia	did not cause pneumonia

- Injected mouse with S strand	mouse dies
- Injected mouse with R strand	mouse lives
- Injected mouse with heat killed S strand	mouse lives
- Injected mouse w/ heat killed S and R strand	*mouse dies*

** He concluded that the R strand was transformed into the S strand

What was the transferring substance???



Oswald Avery

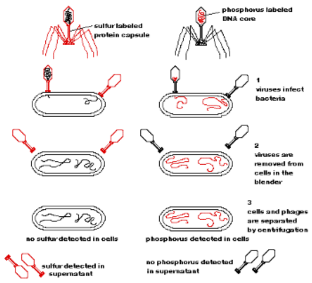
- Identified the molecule that transformed the R strain into the S strain
- Exposed R cells to DNA, protein, and lipids from heat killed S strain
- When the R cells were exposed to S strain DNA, they were transformed
- Avery concluded that when the S strain was heat killed the DNA was released.......some of the R cells incorporated the S DNA → DNA is transferring substance
- Conclusions not accepted by biological community
  - people still thought protein could be genetic material

Hershey and Chase

- published definitive factor that DNA was transforming factor
- Used bacteriophage (a virus that attacks bacteria) in their experiment
  - made up of DNA and protein
  - must inject genetic material into another cell in order to reproduce
- Used Radioactive labeling to track the bacteriophage

group 1	^{32}P = made DNA radioactive
group 2	^{35}S = made protein radioactive

- Group 1 was looked at and the DNA was injected into bacteria
- Group 2 was looked at and the labeled protein was found outside bacteria
- Concluded that DNA was genetic material passed from generation to generation



DNA Structure

- After Hershey-Chase, scientists shifted their focus to the structure of DNA
- 2 types of nucleic acids include : DNA and RNA

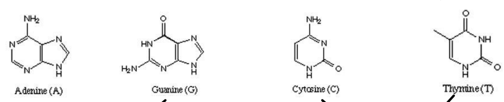
Nucleotides → Building block of DNA/RNA

- subunits of nucleic acids

① sugar ② phosphate ③ Base

** DNA nucleotides are made of... (- Double stranded)
1. the sugar deoxyribose
2. a phosphate group
3. one of four nitrogenous bases

Adenine (A) Guanine (G) Cytosine (C) Thymine (T)

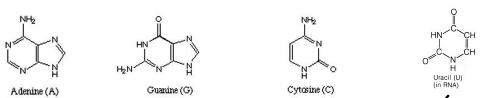


purines (Adenine, Guanine) — pyrimidines (Cytosine, Thymine)

A – T
G – C

** RNA nucleotides are made of... (- single stranded)
1. the sugar ribose
2. a phosphate group
3. one of four nitrogenous bases

Adenine (A) Guanine (G) Cytosine (C) * Uracil (U)



purines (Adenine, Guanine) — pyrimidines (Cytosine, Uracil)

A – U
G – C

Chargaff 's rule

- Erwing Chargaff noticed that the amount of guanine is nearly equal to the amount of cytosine in DNA. He also noticed that the amount of adenine was nearly equal to the amount of thymine

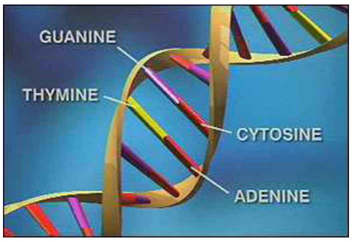
A = T and G = C

Rosalind Franklin

- worked with x-ray diffraction and aimed x-rays at DNA
- her famous photo (photo 51) indicated that DNA was a double helix
  - a twisted ladder shape; two strands of nucleotides twisted around each other

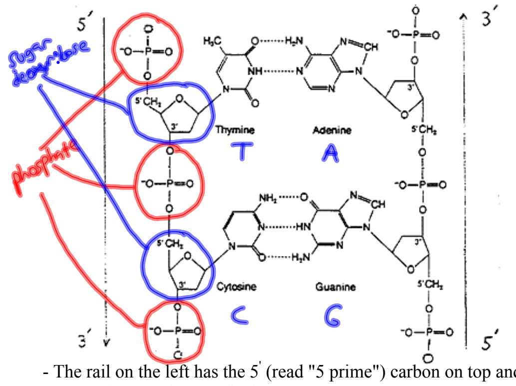
James Watson and Francis Crick

- used Chargaff's data and Franklin's data to build a model of the double helix structure of DNA
- Their model included the following features
  1. two outer strands consist of alternating deoxyribose & phosphate
  2. cytosine and guanine bases pair with one another
  3. adenine and thymine bases pair with one another
- DNA was like a twisted ladder the rungs of the ladder were the base pairs
- a purine base (A &G) always binds with a pyrimidine base (C & T)
- these bases are held together with Hydrogen Bonds
- C = G and A = T so C + G = A + T



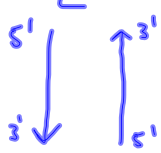
Orientation of DNA Strands

- Carbon molecules can be numbered in organic molecules



- The rail on the left has the 5' (read "5 prime") carbon on top and the 3' (3 prime) carbon on the bottom
  - this strand is oriented 5' to 3'
- The rail on the right has the 3' carbon on the top and the 5' carbon on the bottom
  - this strand is oriented 3' to 5'

** The strand on the left runs in the opposite direction of the strand on the right. This is known as antiparellel orientation.



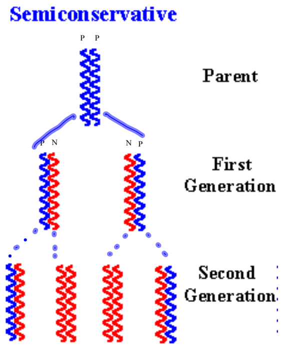
DNA Replication

- DNA replicates and makes copies of itself

* Semiconservative replication *

- a method of replication where parental strands of DNA separate, serve as templates, and produce new DNA molecules
- Each new DNA molecule will have 1 parental DNA strand and 1 new DNA strand
- Has 3 main stages

1. Unwinding 2. Base pairing 3. Joining



Unwinding

- The double helix DNA structure must be unwound or unzipped before replication can take place

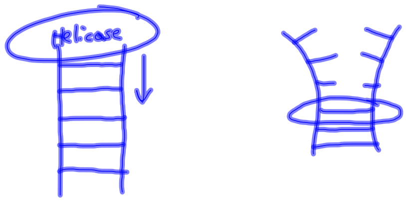
DNA Helicase → an enzyme that is responsible for unwinding DNA

zipper

- once the DNA is unwound, the hydrogen bonds between the bases are broken and we are left with individual strands of DNA

RNA primase → an enzyme that adds a small segment of RNA on each DNA strand

- this small segment of RNA is called an RNA primer



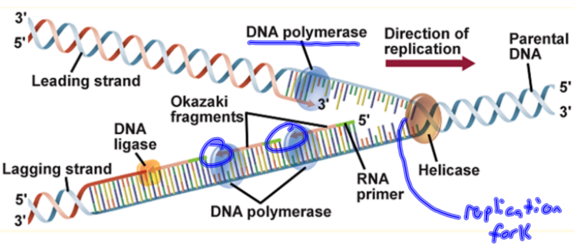
Base Pairing

DNA polymerase → enzyme that attaches to RNA primer and then is responsible for the addition of new nucleotides on the new DNA strands

- DNA polymerase adds new nucleotides to the chain by adding them on to the 3' end of the DNA   works 5' → 3'   5' → 3'   3' ← 5'
- Each base binds to its complement   A - T   C - G

Leading strand - the strand of DNA that is elongated and built continuously as the DNA is unwound

Lagging strand
- the strand of DNA that elongates away from the replication fork.
- It is synthesized discontinuously into small segments called Okazaki fragments.
- DNA polymerase attaches nucleotides 3' to 5' (5' to 3')
- fragments are later connected by an enzyme called DNA ligase



Joining

- When DNA polymerase comes to an RNA primer it replaces the RNA with DNA nucleotides. When the primer is removed, DNA ligase links the DNA sections together

Prokaryotes vs Eukaryotes

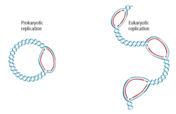
DNA Replication

Eukaryotes

- DNA unwinds in multiple areas as DNA is replicated
- multiple areas of replication are taking place along large chromosomes
- multiple replication origins look like bubbles in the DNA strand

Prokaryotes

- circular DNA strand is opened at one origin of replication
- replication occurs in 2 directions just like eukaryotes



A T G C C C
T A C G G G

T T A G G C T A
A A T C C G A T

How does DNA code for synthesis of proteins???

The basic mechanism for reading and expressing genes is..... central dogma

[DNA —transcription→ RNA —translation→ PROTEIN]

** DNA codes for RNA, which guides synthesis of proteins

RNA

- a nucleic acid that is similar to DNA but contains ribose sugar instead of deoxyribose sugar
- Uracil replaces thymine as one of the bases in RNA AUGC
- RNA is single stranded (DNA is double stranded)

3 Major Types of RNA

* 1. **Messenger RNA (mRNA)**
   - long strands of RNA nucleotides that are formed complementary to one strand of DNA made from DNA
   - mRNA travel from nucleus to ribosome to direct synthesis of specific protein
2. **Ribosomal RNA (rRNA)**
   - RNA that associates with proteins to form ribosomes in the cytoplasm
3. **Transfer RNA (tRNA)**
   - small segments of RNA nucleotides that transport amino acids to the ribsosome

Transcription DNA → mRNA

- the synthesis of mRNA from DNA
- the DNA code is transferred to mRNA in the nucleus

Steps of Transcription

1. The DNA is unzipped in the nucleus (Helicase)
2. RNA polymerase binds to a section of the DNA where mRNA will be produced
3. RNA polymerase moves along the DNA 3' to 5'
4. The DNA strand read by the RNA polymerase is called the *template strand*
5. mRNA is synthesized complementary to the template strand
6. the new mRNA moves out of the nucleus and into the cytoplasm

DNA template strand: T A A C T G C
mRNA strand: A U U G A C G

DNA template strand: T G C A C A G
mRNA strand: A C G U G U C

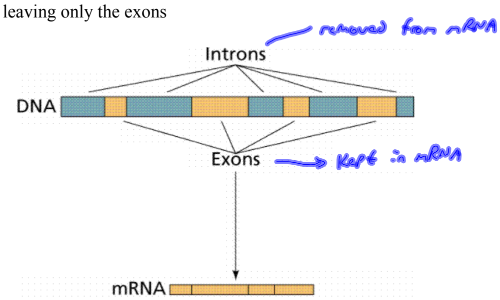
Introns and Exons

- mRNA is shorter than DNA

Introns → sequences that are not included in the final mRNA

Exons → coding sequences that remain in the final mRNA

- the introns are removed from the mRNA before it leaves the nucleus leaving only the exons



DNA A T T T G C A A C G C T T A T G

mRNA U A A A C G U U G C G A A U A C

The Code

- Scientists knew that there are 20 amino acids so they knew that the DNA must provide at least 20 codes

- It was discovered that it took 3 DNA or RNA bases to code for 1 amino acid

1 amino acid = 3 bases

Codon = the 3 base code in DNA or mRNA

- Each of the 3 bases in a DNA codon is transcribed into mRNA

- the mRNA is then used to identify the correct amino acid

Second base of codon

First base of codon (5' end)	U	C	A	G	Third base of codon (3' end)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
U	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
U	UUA Leu	UCA Ser	UAA	UGA	A
U	UUG Leu	UCG Ser	UAG	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
C	CUC Leu	CCC Pro	CAC His	CGC Arg	C
C	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
C	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
A	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
A	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
A	AUG Met	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
G	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
G	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
G	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

AUG = methionine ⟶ start codon

UAA, UAG, and UGA ⟶ stop codon

code is redundant - more than 1 codon can ... to same amino acid

GGG CAA TAG TAC GGG ACA ATT DNA

CCC | G UU | AUG | AUG | CCC | UGU | UAA | RNA

Translation

mRNA → protein

- once the mRNA is processed it moves out of the nucleus and to the ribosome

Ribosome structure — make protein

- Consist of a large ribosome unit and a small ribosome

Translation

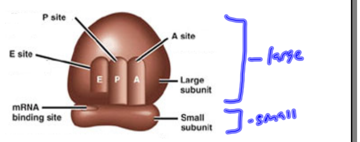
1. The large and small ribosome units come together and attach to mRNA

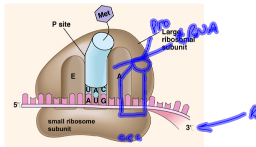
2. a tRNA with the anticodon and attached amino acid will move in and bind to the mRNA at the P site of the ribosome

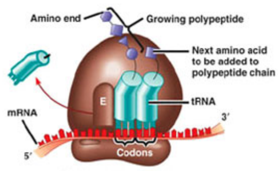
3. Another tRNA attached to an amino acid will move into the A site of the ribosome. This will be the next amino acid in the chain

4. Once the amino acids are attached in the P site, the tRNA moves to the E site. This is where the tRNA leaves the ribosome

5. The ribosome continues to move along the mRNA making a long chain of amino acids until a stop codon reaches the A site in the ribosome







Eukaryote Gene Regulation

- Gene regulation is crucial during development of eukaryotic organisms

- Cells go through a process called differentiation where cells become specialized to do a specific thing

HOX genes control this differentiation. They help determine the body plan of an organism

Mutations

- A mutation is a permanent change that occurs in a cell's DNA

- Mutations can range from changes in a single base pair to deletions of large pieces of chromosomes

Point Mutations

AATGCCGAT
AATCCCGAT

When one base is exchanged for another. This is called a substitution

Frameshift Mutations

When insertions or deletions cause a shift in the entire frame of an amino acid sequence

normal AATGCCGAT
insert. AATTGCCGAT
delete AATGCGAT

- Sometimes point mutations will not lead to any type of change because the code for different amino acids is redundant

EX.	
DNA code ------ ATA	DNA code ---- ATG
RNA code ------ UAU	RNA code ---- UAC
Amino Acid ---- Thr	Amino Acid -- Thr

Types of Mutations

1. Missense (substitution) - the code is changed and the wrong amino acid is produced

Normal code ** THE BIG FAT CAT ATE THE WET RAT
Missense code ** THE BIZ FAT CAT ATE THE WET RAT

- Achondroplasia

2. Nonsense (substitution) - the code is changed to a stop codon and the protein is stopped from being made

Normal code ** THE BIG FAT CAT ATE THE WET RAT
Nonsense code ** THE BIG RAT

- Muscular Dystrophy

3. Deletion (causing frameshift) - a base is deleted and this changes the multiples of 3 codons

Normal code ** THE BIG FAT CAT ATE THE WET RAT
Deletion ** THB IGF ATC ATA TET HEW ETR AT

- Cystic Fibrosis

4. Insertion (causing frameshift) - a base is inserted and this changes the multiples of 3 codons

Normal code ** THE BIG FAT CAT ATE THE WET RAT
Insertion ** THE BIG ZFA TCA TAT ETH EWE TRA

- Crohn's disease

5. Expanding Mutations - tandem repeats of codons

Normal code ** THE BIG FAT CAT ATE THE WET RAT
Generation 1 ** THE BIG FAT CAT CAT CAT ATE THE WET RAT
Generation 2 ** THE BIG FAT CAT CAT CAT CAT CAT CAT ATE THE WET RA

- Huntington's disease

Causes of Mutations

- Point Mutations can occur spontaneously when DNA is being replicated

Mutagens - substances that cause mutations

- some chemicals and radiation can damage DNA
- X-rays, gamma rays, Ultraviolet Rays