Unit 1 DNA & the Genome

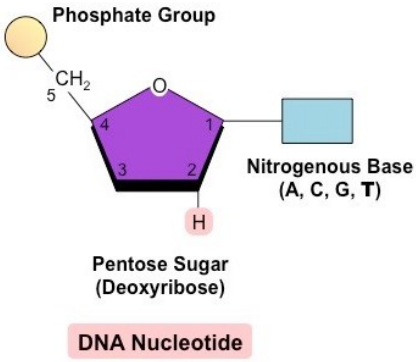
Key Area 1 : Structure of DNA

- DNA is a double-helix consisting of repeating units of **DNA nucleotides**.
- A DNA nucleotide consists of 3 components:

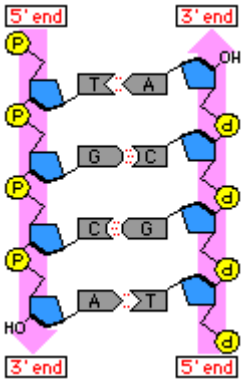
  Deoxyribose sugar

  Organic Base

  Phosphate group



- The 2 DNA strands in the double helix are **anti-parallel**.
- There is a **Deoxyribose sugar at the 3' end** and a **Phosphate group at the 5' end**.



- The DNA nucleotides in a strand of DNA are joined together by **strong chemical bonds** between the phosphate group of one nucleotide and the deoxyribose sugar of another nucleotide. This creates a **sugar-phosphate backbone**.
- The is complimentary base-pairing between the 2 strands in the double helix.

A=T

There are 2 **weak Hydrogen bonds** between Adenine and Thymine

C≡G

There are 3 weak hydrogen bonds between Cytosine and Guanine.

Organisation of DNA

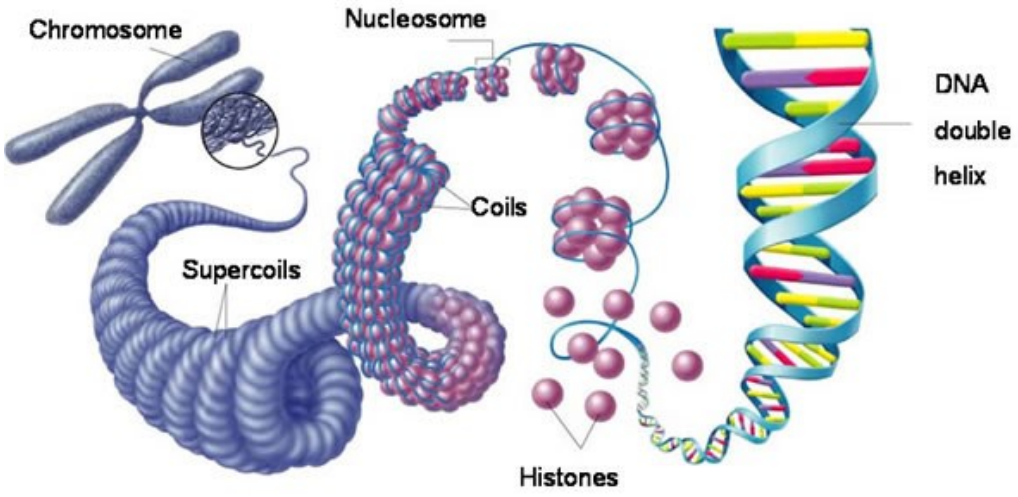
DNA is found in **LINEAR CHROMOSOMES** in the **nucleus** of **EUKARYOYES**. Eukaryotes have a nucleus present in their cells (e.g. plant, animal & fungal cells). Prokaryotes do not have a nucleus (e.g. Bacteria).

DNA is found in **CIRCULAR CHROMOSOMES** in the **cytoplasm of PROKARYOTES** and in **Mitochondria and Chloroplasts of Eukaryotes**.

DNA is found in **PLASMIDS** in the cytoplasm of **PROKARYOTES and YEAST** cells.

Type of Cell	Linear Chromosomes	Circular Chromosomes	Plasmids
Animal	✓	✓	
Plant	✓	✓	
Bacterial		✓	✓
Fungal	✓	✓	✓Yeast only

DNA is **tightly coiled & packaged** with associated **Histone Proteins**.

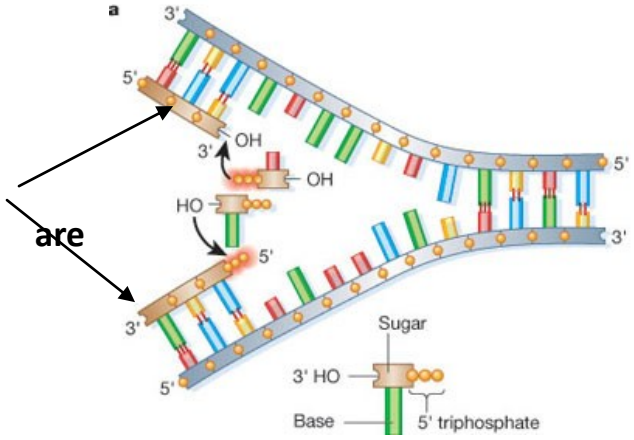


Key Area 2 Replication of DNA

Prior to cell division, DNA is replicated by **DNA Polymerase.**

DNA Polymerase needs PRIMERS to start replication. A Primer is a short strand of nucleotides which binds to the 3' end of the template DNA strand allowing the DNA Polymerase to add DNA Nucleotides.

Primers **are**



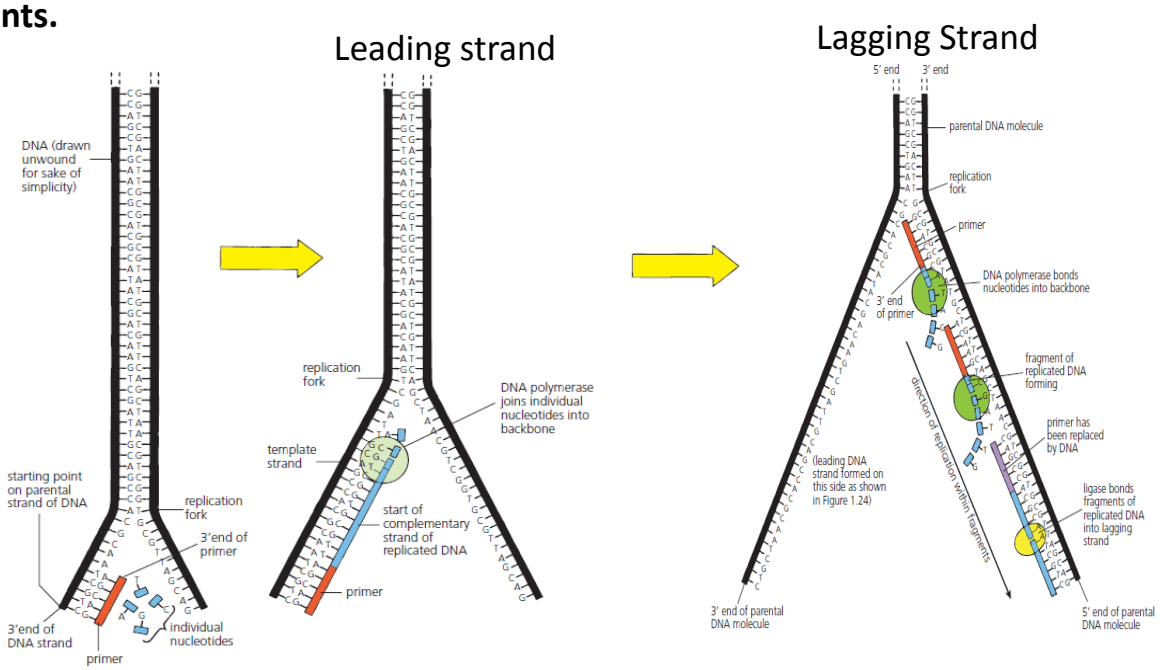
DNA is **unwound** (by DNA Polymerase) and **Hydrogen bonds between the bases broken** to form 2 template strands.

DNA Polymerase adds DNA Nucleotides, using complimentary base pairing, to **the deoxyribose (3') end of the new DNA strand** which is forming.

DNA Polymerase can only add DNA Nucleotides in one direction, resulting in the **Leading Strand being replicated continuously** and the **Lagging Strand being replicated in Fragments.**

Leading strand

Lagging Strand



Fragments of DNA on the Lagging strand are joined together by **LIGASE.**

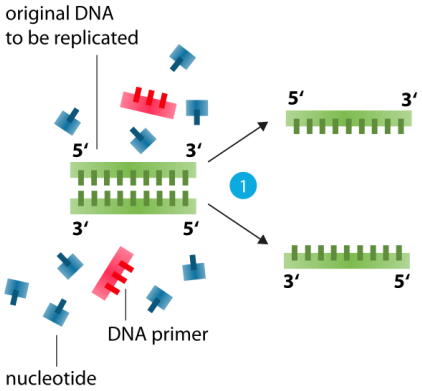
Polymerase Chain Reaction (PCR)

PCR **AMPLIFIES DNA** using complimentary primers for specific target sequences.

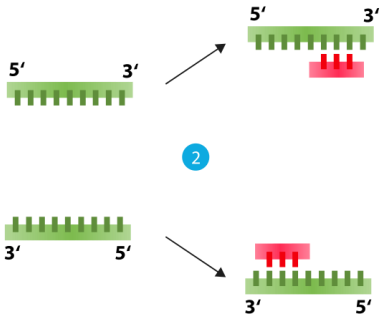
In PCR, primers are short strands of nucleotides which are complimentary to specific target sequences at the 2 ends of the region of DNA to be amplified.

Repeated cycles of **HEATING & COOLING** amplify the target region of DNA.

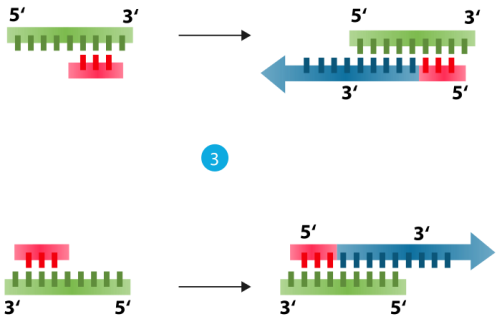
1. **DNA is heated to between 92 and 98°C to separate the strands**.



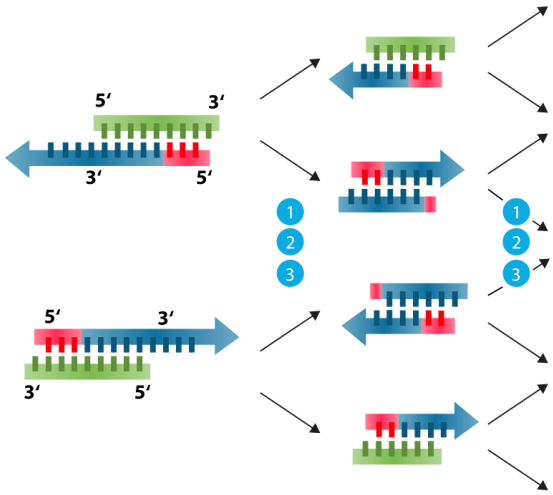
2. **It is then cooled to between 50 and 65°C to allow Primers to bind to target sequences.**



3. **It is then heated to between 70 and 80°C for HEAT-TOLERANT DNA Polymerase to replicate the region of DNA.**



4. The cycle is then repeated.



Each cycle DOUBLES the amount of DNA present.

Example:

1 copy	→	2	→	4	→	8	→	16	→	32	→	64	→	128 copies
	Cycle 1		Cycle 2		Cycle 3		Cycle 4		Cycle 5		Cycle 6		Cycle 7	

After 7 PCR Cycles, 128 copies of the original DNA target sequence are produced.

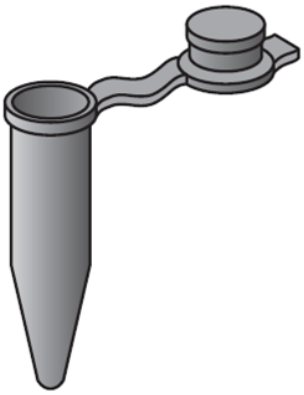
Requirements for PCR

PCR requires:

1. **A DNA Template**
2. **A Supply of the 4 types of DNA Nucleotides (A,T,C &G)**
3. **Primers**
4. **Heat-tolerant DNA Polymerase (enzyme)**
5. **A pH Buffer (to create optimum conditions for enzyme activity)**

Contents of tube

– DNA
– DNA nucleotides
– primers
– enzyme and buffer



Practical Applications of PCR

PCR can amplify DNA for use in the following applications:

1. To help **SOLVE CRIMES** (Forensic evidence).
2. Settle **PATERNITY SUITS**
3. **Diagnose Genetic Disorders.**

Unit 1 DNA & the Genome

Key Area 3: Gene Expression

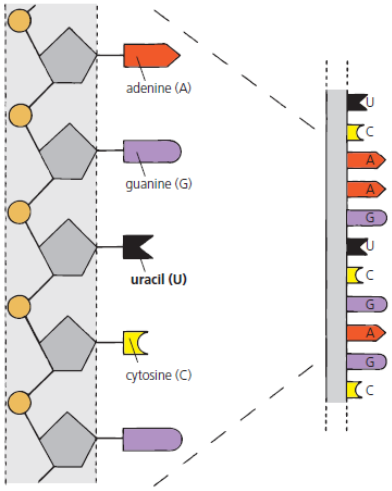
Gene Expression involves the **transcription and translation** of DNA sequences.

Only a fraction of the genes in a cell are expressed.

Transcription and translation involves **3 types of RNA: mRNA, tRNA and rRNA.**

RNA is **single stranded** and is composed of nucleotides containing Ribose sugar, phosphate and 1 of 4 bases : **Cytosine, Guanine, Adenine and Uracil** (there is no Thymine in RNA, Uracil replaces this).

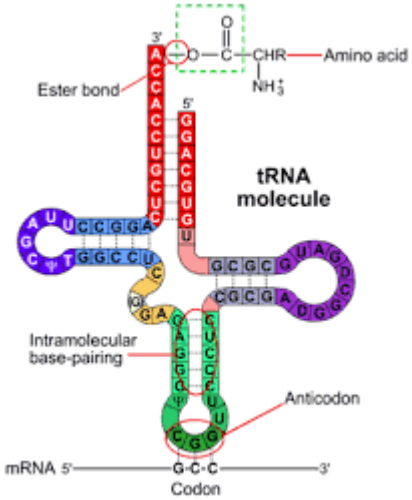
mRNA



Messenger RNA (mRNA) carries a copy of the DNA code from the nucleus to the Ribosome.

Each triplet of bases on the mRNA molecule is called a CODON and codes for a specific amino acid.

tRNA



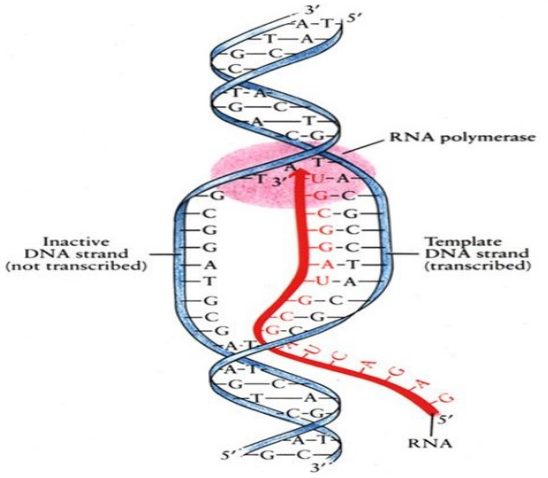
tRNA folds due to complementary base pairing. Each tRNA molecule carries its specific amino acid to the ribosome.

A tRNA molecule has an anticodon (an exposed triplet of bases) **at one end and an attachment site for a specific amino acid at the other end.**

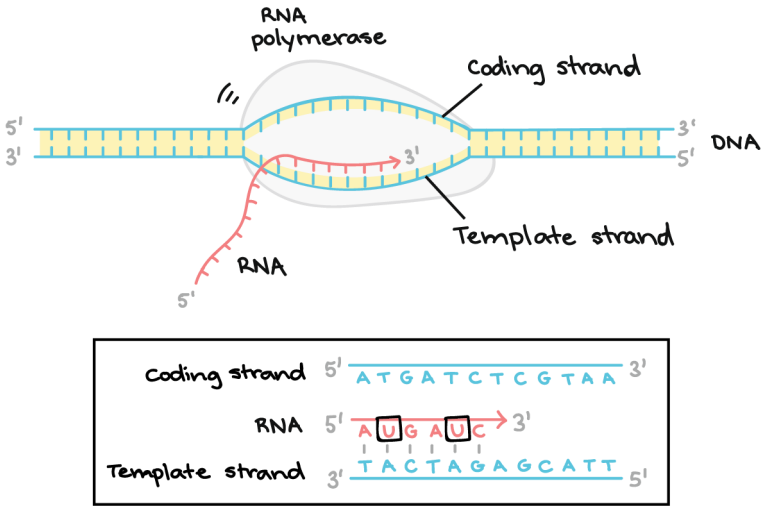
Ribosomal RNA (rRNA) and Proteins are used to form the Ribosome.

TRANSCRIPTION

The enzyme **RNA POLYMERASE** moves along DNA **UNWINDING** the double helix and **breaking the hydrogen bonds between the bases**.



RNA Polymerase synthesises a **PRIMARY mRNA TRANSCRIPT** from RNA Nucleotides by complimentary base pairing.



Uracil in RNA is complimentary to Adenine.

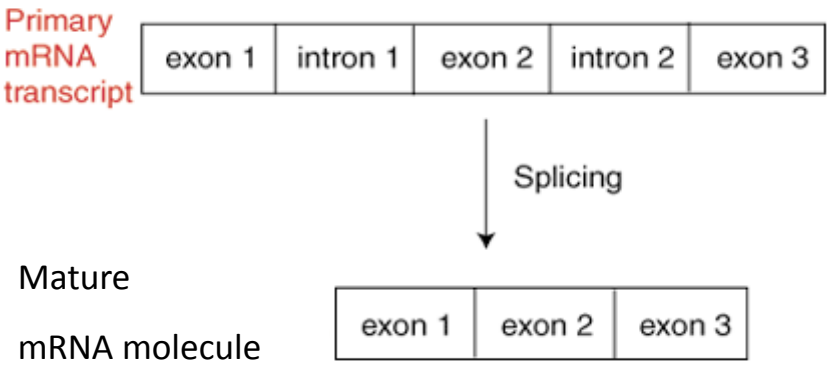
Example	DNA Template	TAC TAG AGC ATT CGG TCC AAG
	Primary mRNA transcript	AUG AUG UCG UAA GCC AGG UUC

RNA SPLICING

Some of the DNA which is transcribed (copied) is **NON-CODING** (does not contain the information required to produce a protein) and therefore these regions known as **INTRONS** must be removed from the Primary mRNA Transcript.

Clue : NICE (Non-coding Introns, Coding Exons)

RNA Splicing involves the **removal of the NON-CODING INTRONS** and joining together (Splicing) of the **CODING regions known as EXONS.**

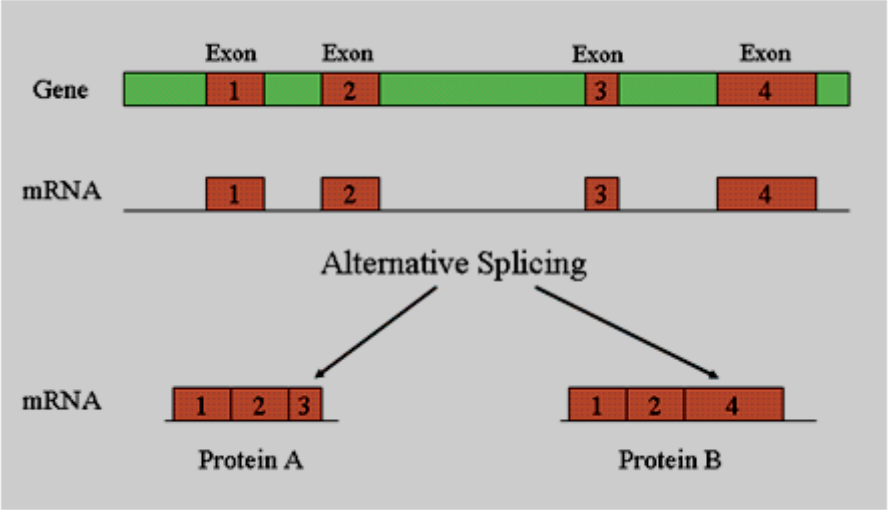


The order of Exons is UNCHANGED during Splicing.

ALTERNATIVE RNA SPLICING

Different Proteins can be expressed from **ONE GENE** as a result of **Alternative RNA Splicing.**

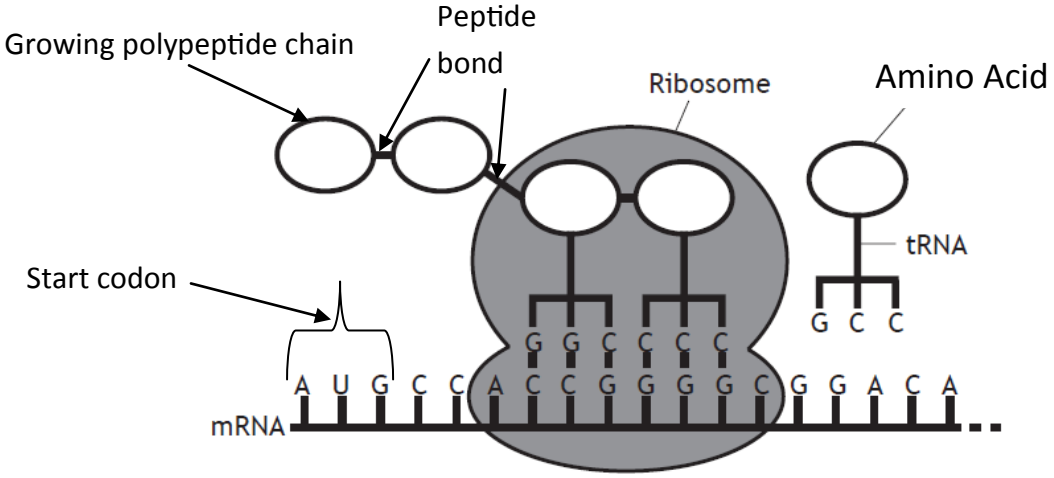
Different mature mRNA transcripts are produced from the same primary transcript **depending on which exons are retained**.



TRANSLATION

tRNA is involved in the **translation of mRNA** into a **Polypeptide** at a **Ribosome.**

Translation begins at a **START CODON** and ends at a **STOP CODON.**



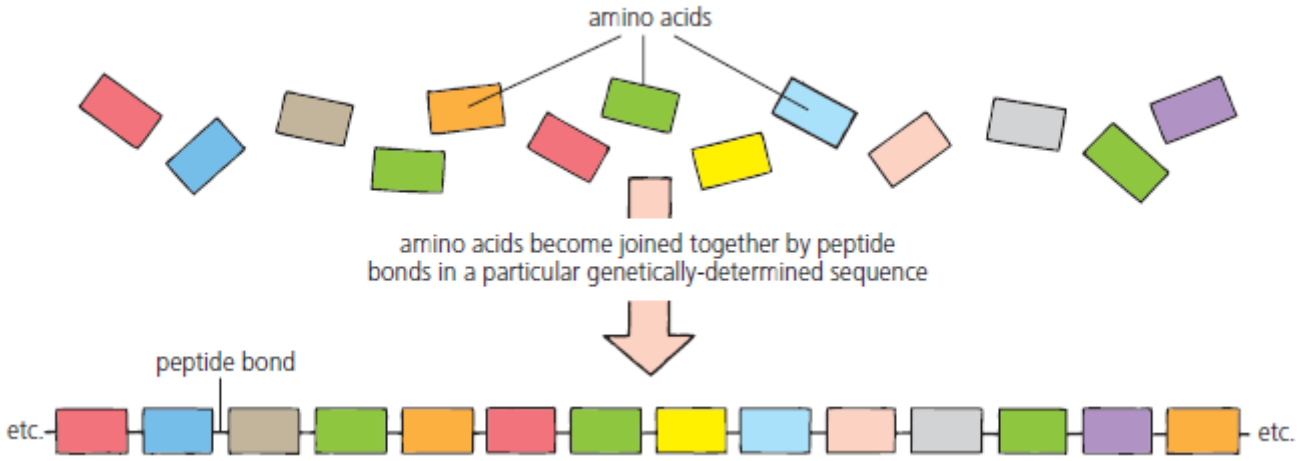
Anticodons bond to Codons by complimentary base pairing, translating the genetic code into a sequence of **Amino Acids.**

Peptide Bonds join the amino acids together.

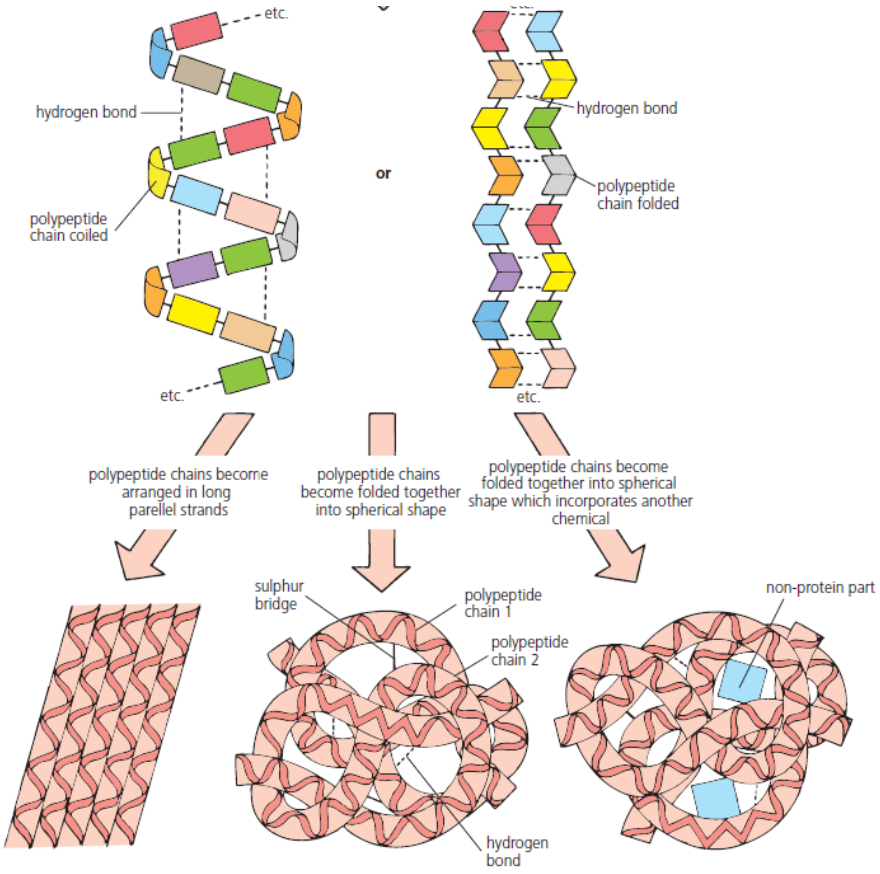
Each tRNA then leaves the Ribosome as the Polypeptide is formed.

STRUCTURE OF PROTEINS

Amino Acids are linked by **PEPTIDE BONDS** to form **POLYPEPTIDES**.



Polypeptide Chains **FOLD** to form the 3-Dimentional shape of a Protein, held together by **HYDROGEN BONDS** and other interactions between individual amino acids.



Proteins have a large variety of **shapes which determines their functions**.

Phenotype is determined by the proteins produced as the result of Gene Expression.

Environmental factors also influence phenotype.

Unit 1 DNA & the Genome

Key Area 4 : Cellular Differentiation

Cellular Differentiation is the process by which a cell **expresses certain genes** to produce **PROTEINS** characteristic for that type of cell. This allows a cell to carry out specialised functions.

STEM CELLS

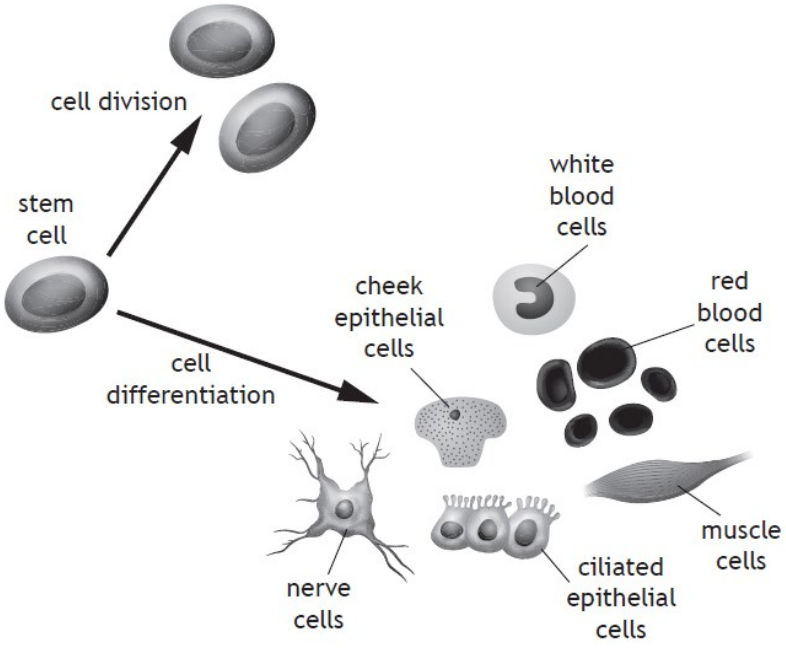
Stem cells are **UNSPECIALISED CELLS** in animals that can **divide (SELF-RENEW)** and/or **Differentiate.**

There are 2 Types of Stem Cells : **Embryonic and Tissue**

EMBRYONIC STEM CELLS

EMBRYONIC stems cells can differentiate into **ALL THE CELL TYPES** that make up the organism and so are **PLURIPOTENT.**

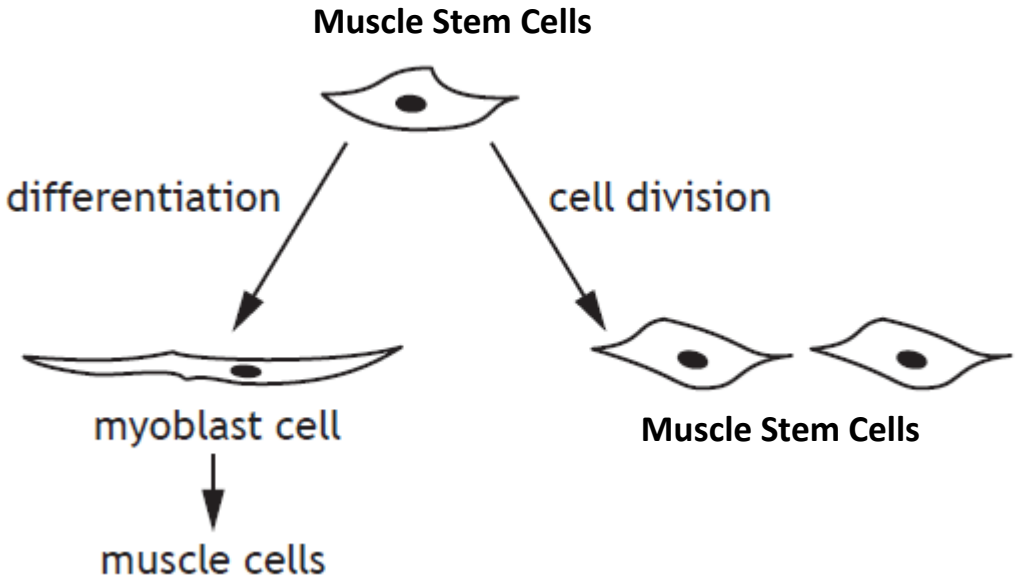
Example



All the genes in embryonic stem cells can be **switched on** so these cells can differentiate into **ANY TYPE OF CELL.**

TISSUE STEM CELLS

TISSUE stem cells are involved in the **GROWTH, REPAIR** and **RENEWAL** of the cells found in that tissue. They are **MULTIPOTENT** because they can differentiate into all of the types of cell found in a particular tissue type.



THERAPEUTIC AND RESEARCH USES OF STEM CELLS

Therapeutic uses of stem cells involve the **repair of damaged or diseased organs or tissues**.

Stem cells from the embryo can self-renew, under the right conditions in the lab.

Examples :

Stem cells can be used to repair damaged CORNEA in the eye.

Stem cells can be used to regenerate SKIN tissue for BURNS VICTIMS.

Research uses of stem cells involves them being used as **model cells** to **study how diseases develop** or being used for **drug testing**.

Stem cell research provides information on how **cell processes** such as **cell growth**, **differentiation** and **gene regulation** work.

ETHICAL ISSUES

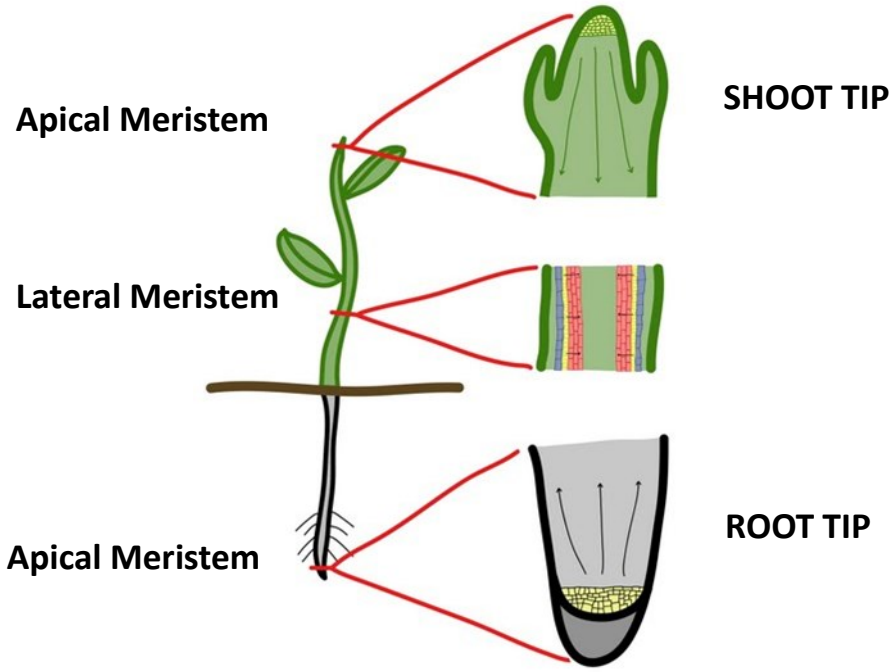
Use of EMBRYONIC stem cells can offer effective treatments for disease and injury, however, it involves **destruction of embryos** and therefore the **destruction of a potential life**.

MERISTEMS

Meristems are regions of **unspecialised cells in plants** that can **divide (self-renew) and/or differentiate.**

Apical meristems are found in the **Root Tip & Shoot Tip.** These give rise to increase in length/height.

Lateral meristems, also known as **Cambium,** are found in vascular bundles between the Xylem & Phloem**.** These give rise to **Thickening** of the plant.



Unit 1: DNA & the Genome

Key Area 5 : The Structure of the Genome

The **Genome** of an organism is it's **entire hereditary information encoded in DNA**.

A genome is made up of **GENES** and other **DNA sequences that do not code for proteins**. Most of the eukaryotic genome consists of non-coding sequences.

Genes

DNA sequences that **code for protein** are defined as **GENES**. These sequences are transcribed to produce the Primary mRNA transcript during protein synthesis.

Non-coding Sequences

Other sequences that **do not code for protein** can either

- **regulate transcription**

or are

- **transcribed but never translated**. E.g **tRNA and rRNA** are non-translated forms of RNA.

Exam Style Question

Which line in the table below shows features of the human genome?

	Contains base sequences that regulate transcription	*Contains base sequences transcribed to RNA but never translated*	*Contains base sequences from which primary transcripts are produced*
A	✗	✓	✗
B	✗	✗	✓
C	✓	✓	✗
D	✓	✓	✓

In the above example, **D is the correct** answer because the Genome contains DNA sequences that **regulate transcription** AND sequences that are **transcribed to RNA but never translated** (tRNA and rRNA) AND sequences **from which primary transcripts are produced** (GENES).

Unit 1: DNA & the Genome

Key Area 6: Mutations

Mutations are **changes in the DNA** that can result in **no protein** or an **altered protein** being synthesised.

SINGLE GENE MUTATIONS

A **Single Gene mutation** involves the **alteration of a DNA nucleotide sequence** as a result of:

- **substitution**
- **Insertion**
- **Deletion**

of Nucleotides.

Clue : DIGS

Deletion

Insertion

Gene

Substitution

Substitution Mutations

These involve one DNA nucleotide being swapped/substituted for another.

Missense, Nonsense and Splice-site mutations are all examples of substitution mutations.

Missense mutations result in **one amino acid being changed for another**. This may result in a **non-functional protein** or **have little effect on the protein**.

Example 1

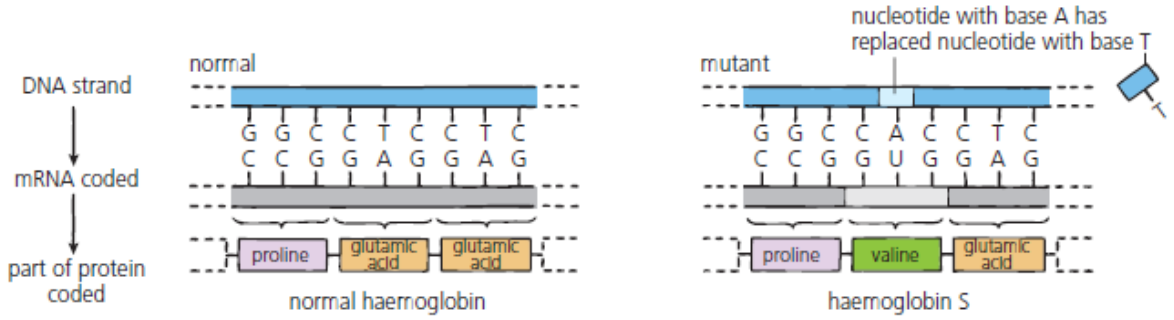
Normal DNA Sequence : …. A T G T C C A T G….

Missense mutation : …. A T G G C C A T G….

This may have **NO EFFECT** on the protein produced if the codon GCC leads to the transcription & translation of an amino acid with similar chemical properties to the amino acid coded for by the original sequence. This means that the folding of the protein produced is unchanged and therefore the protein will have a similar shape & function to the original protein.

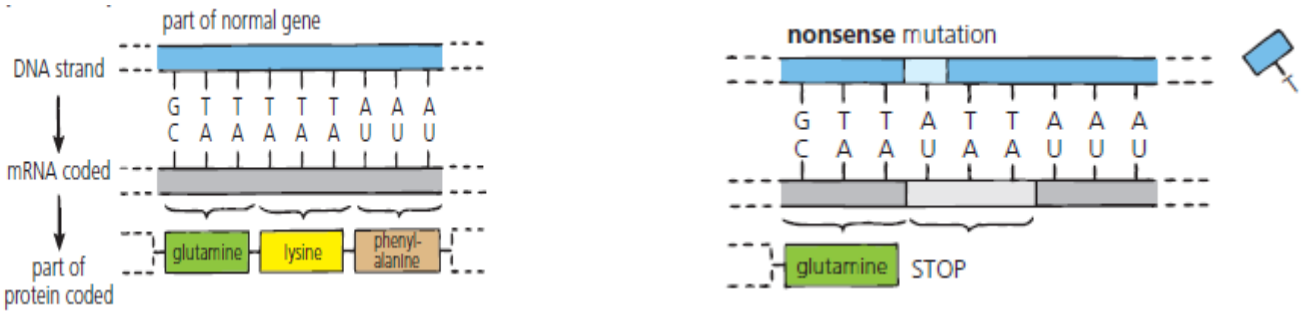
Example 2

Sickle-cell Anaemia



This missense mutation results in a protein which does not function properly since the amino acid (Valine in this case) has **different chemical properties** to the original amino acid (Glutamic Acid).

Nonsense mutations result in a premature STOP CODON being produced which results in a shorter protein.

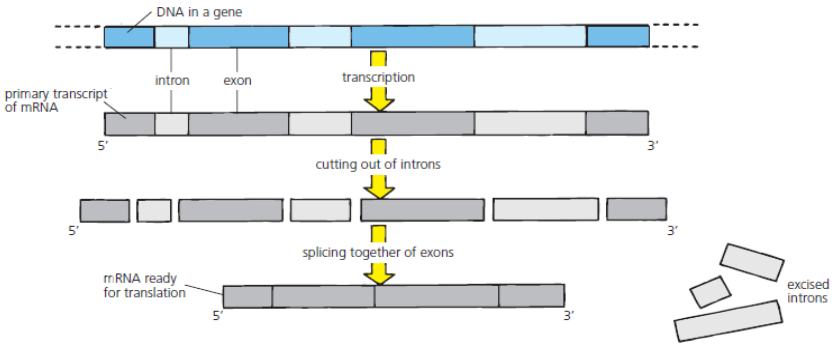


In the above example, substitution of the nucleotide carrying Thymine with a nucleotide carrying Adenine means that during translation, the codon UAA on the mRNA represents a STOP codon and so translation comes to an end, leading to a much shorter protein being produced.

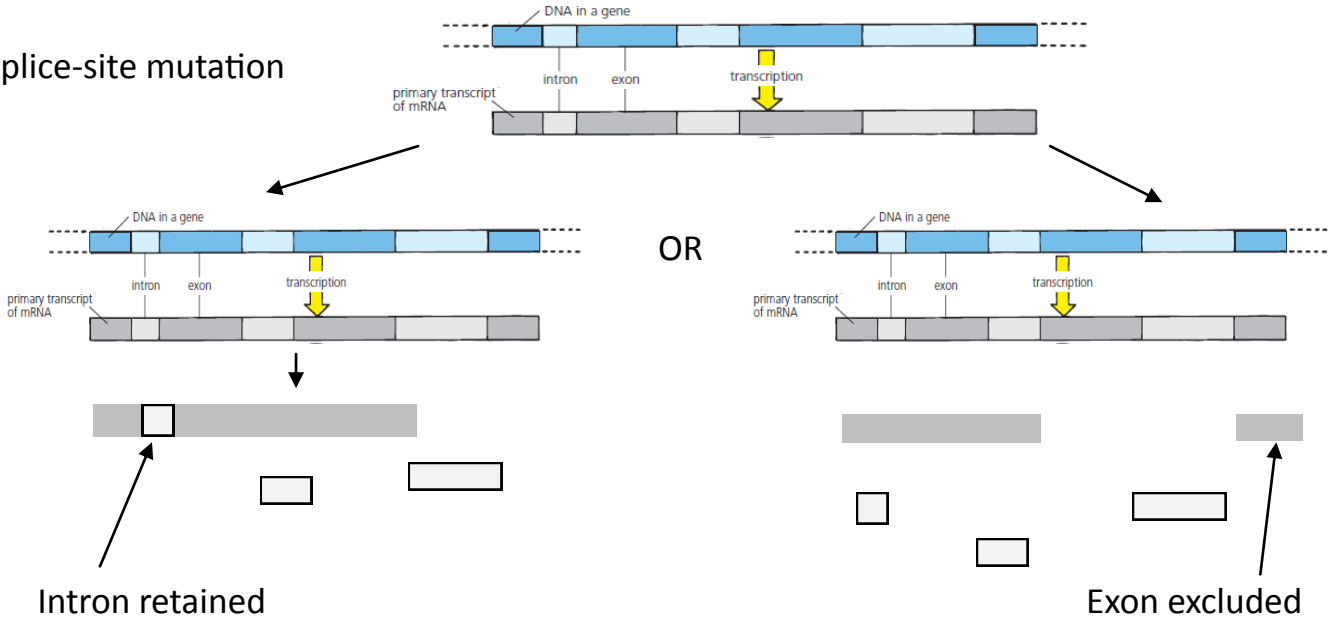
Splice-site mutations result in some **INTRONS being RETAINED** and/or some **EXONS not being INCLUDED** in the mature mRNA transcript.

E.g

Normal



Splice-site mutation



Intron retained

Exon excluded

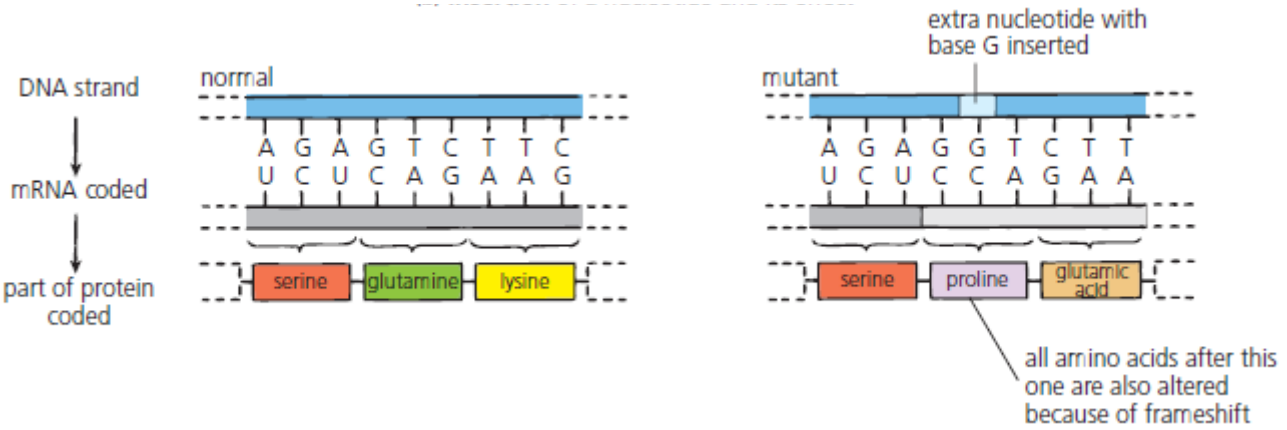
Insertion Mutations involve an extra **DNA nucleotide** being **added/inserted** into the DNA sequence.

Deletion Mutations involve a **DNA nucleotide** being **left out/deleted** from the DNA sequence.

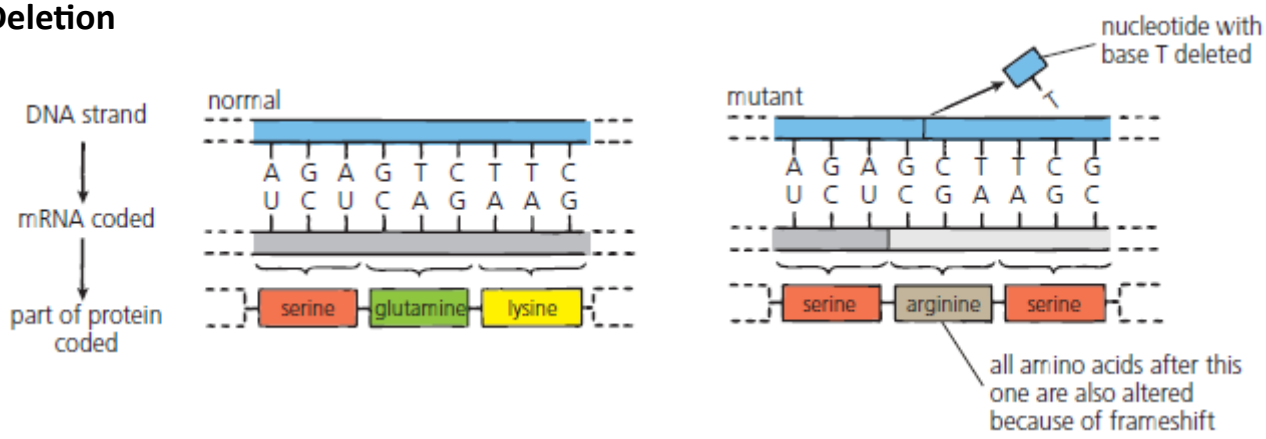
Both **Insertion and Deletion** mutations result in a **Frame-shift**.

Frame-shift mutations cause **ALL** of the **codons** and all of the **amino acids** after the mutations to be changed. This has a major effect on the structure of the protein produced.

Insertion



Deletion



CHROMOSOME MUTATIONS

A Chromosome mutation involves a change in the **structure** or **number** of **chromosomes**.

There are 4 types of chromosome mutations:

- **Deletion**
- **Inversion**
- **Translocation**
- **Duplication**

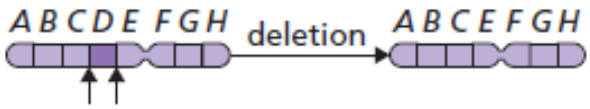
Clue : DICTD

Where C stands for Chromosome

The **substantial changes** in chromosome mutations often make them **lethal**.

Deletion

This is where a **section of chromosome is removed**.

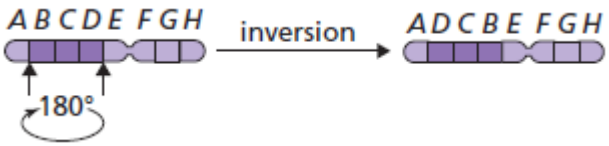


Each letter represents a GENE.

So, in this case Gene D has been deleted.

Inversion

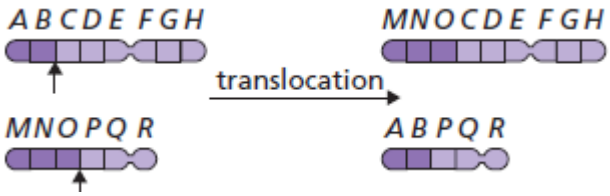
This is where a **section of chromosome is reversed**.



The chromosome breaks in 2 places and a set of genes rotates through 180^{o}

Translocation

This is where a **section of a chromosome is added to a different chromosome**, **not it's homologous partner**.



Duplication

This is where a **section of a chromosome** is **added from it's homologous partner**.

Some duplications can be highly detrimental whilst others can be important in evolution.

IMPORTANCE OF MUTATIONS & GENE DUPLICATIONS IN EVOLUTION

Duplication allows potential beneficial mutations to occur in a duplicated gene whilst the original gene can still be expressed to produce it's protein.

Unit 1: DNA & the Genome

Key Area 7: Evolution

Evolution involves the changes in organisms over generations as a result of genome variations.

Selection

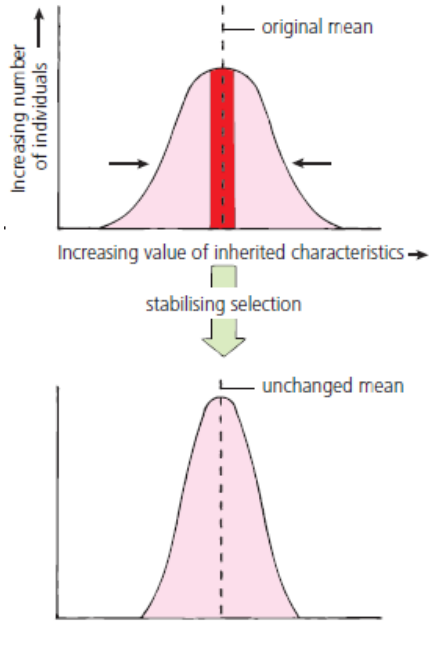
Natural Selection

This is the **non-random increase in frequency of DNA sequences** that **increase survival** and the **non-random reduction in the frequency of deleterious sequences**.

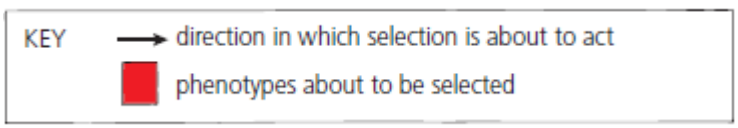
The **changes in phenotype frequency** will be due to one of the following types of natural selection:

- **Stabilising**
- **Directional**
- **Disruptive**

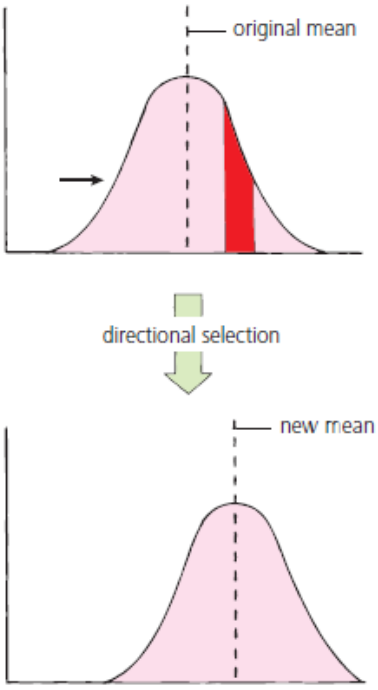
Stabilising selection occurs when the **average phenotype is selected for** and **extremes of the phenotype range are selected against**.



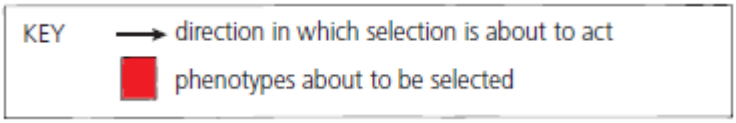
When natural selection has a stabilising effect, the **mean phenotype remains unchanged** but the **range of phenotypes is narrower.**



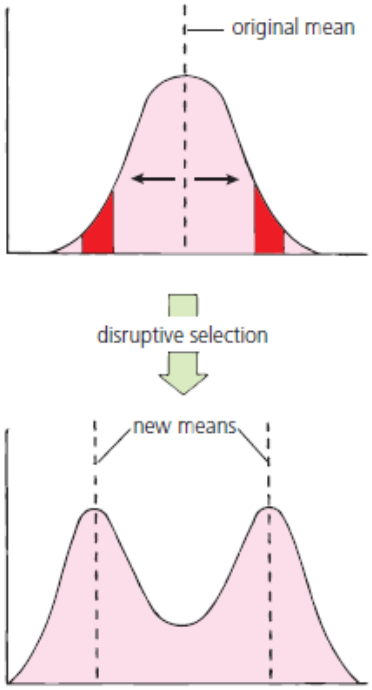
Directional selection occurs when **one extreme of the phenotype range is selected for**.



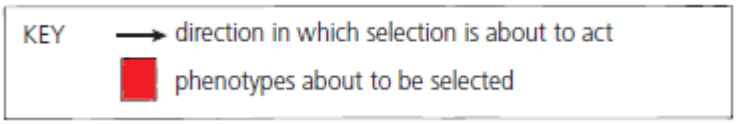
When natural selection has a directional effect, the **mean phenotype and range of phenotypes change.**



Disruptive selection occurs when **2 or more phenotypes are selected for**.



When natural selection has a disruptive effect, **2 new mean phenotypes result** and the **range of phenotypes is altered**.

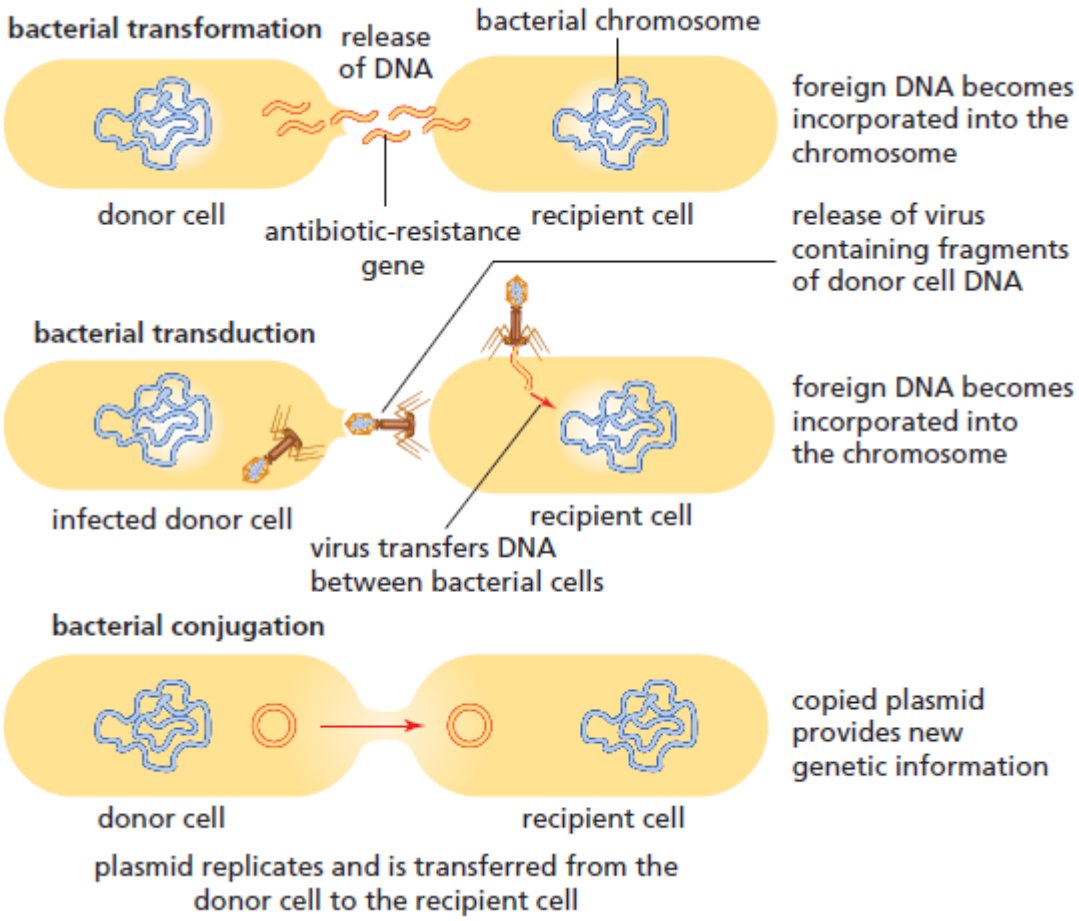


Natural Selection in Prokaryotes

Natural Selection in prokaryotes is **more rapid**.

Prokaryotes can exchange genetic material (genes) **horizontally**, resulting in faster evolutionary change than organisms that only use vertical gene transfer (from parent to offspring/one generation to the next)

Horizontal gene transfer is where **genes are transferred between individuals in the same generation**.



(From August 2018 you do not need to know the methods of horizontal gene transfer)

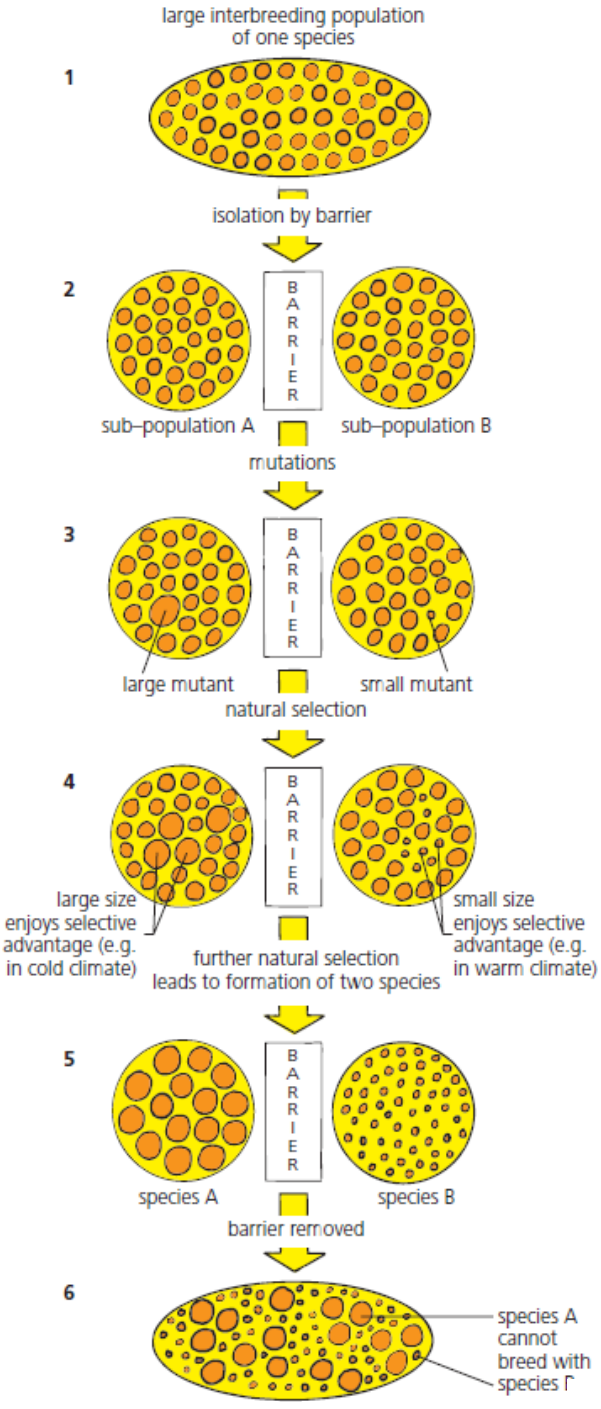
Vertical Gene Transfer is where genes are transferred from **parent to offspring** (different generation) as a result of **sexual or asexual reproduction**.

Speciation

A **species** is a **group of organisms capable of interbreeding** and **producing fertile offspring**, and which does not normally breed with other groups.

Speciation is the **generation of new biological species by evolution** as a result of:

- **Isolation**
- **Mutation**
- **Selection**



Initial **large interbreeding population** of one species, **sharing genes**.

An **Isolation barrier** splits the original population into **sub-populations** and **prevents gene flow** between the sub-populations.

A **different mutation** occurs in each sub-population.

Some **mutations may be favourable** and are **selected for** by **natural selection**.

After **many generations**, the frequency of the mutation increases in each sub-population.

After a **very long time**, the 2 sub-populations are now so genetically different that they can **no longer interbreed to produce fertile offspring**

i.e **2 separate species.**

The **type of Isolation** barrier determines the type of Speciation which occurs.

Geographical barriers (e.g. mountain range, desert, river, sea) lead to **Allopatric Speciation.**

Behavioural or Ecological barriers lead to **Sympatric Speciation.**

In Sympatric speciation the behavioural or ecological barriers prevent gene flow between populations living side by side but do not interbreed and so natural selection is able to act separately on the 2 sub-populations.

Unit 1: DNA & the Genome

Key Area 8: Genomic Sequencing

In genomic sequencing the **sequence of nucleotide bases** can be determined for **individual genes and entire genomes**.

Computer programs can be used to identify base sequences by looking for sequences similar to known genes.

To compare sequence data, **computer and statistical analyses** (bioinformatics) are required.

Many genomes have been sequenced, particularly of **disease-causing organisms, pest species and species that are important model organisms for research**.

Comparison of genomes from different species has revealed that **many genes are highly conserved** across different organisms.

PHYLOGENETICS

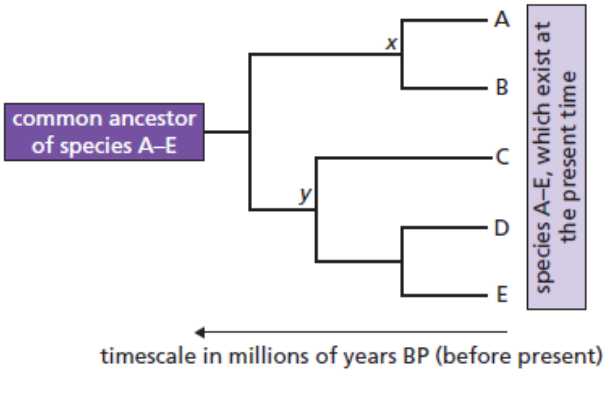
Phylogenetics is the study of evolutionary history and relationships.

EVOLUTIONARY RELATEDNESS

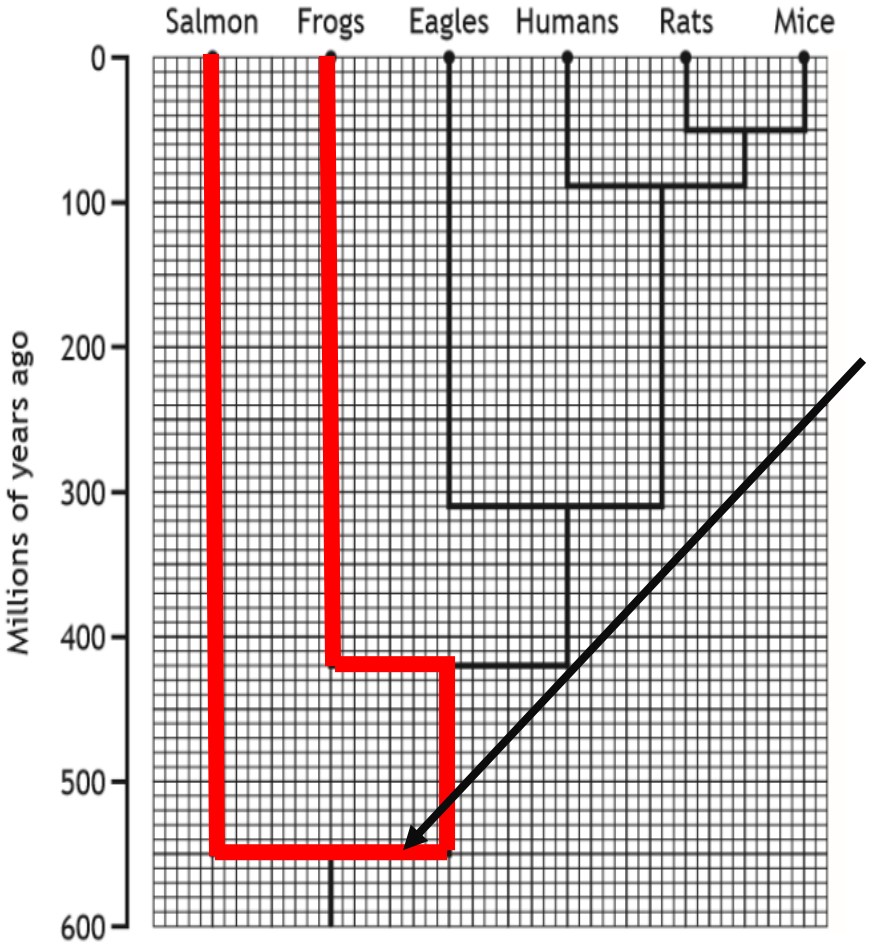
The **sequence of events in EVOLUTION** and **EVOLUTIONARY RELATEDNESS amongst groups of organisms** can be determined using:

- **Sequence data**
- **Fossil evidence**

Sequence divergence (mutations leading to changes in DNA sequence data) can be used to estimate time since lineages diverged.

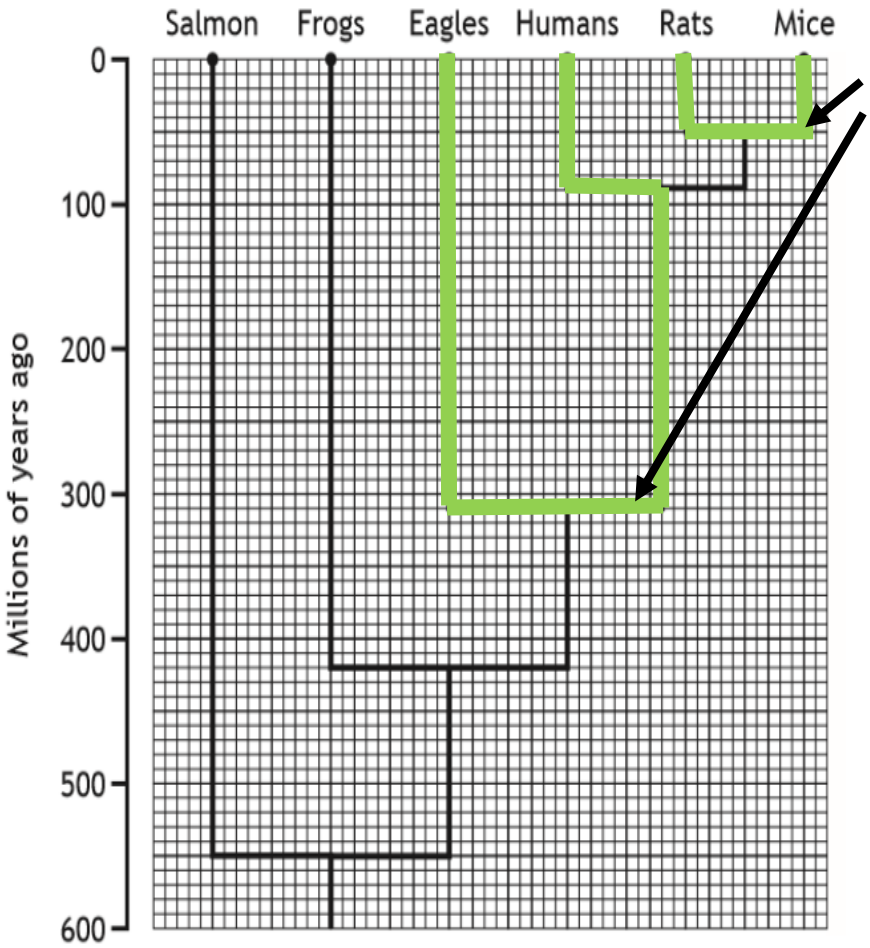


Exam style question



To estimate how long ago the common ancestor of Salmon and Frogs lived you trace the lines to where they meet as shown.

In this example, the Salmon and Frogs shared a common ancestor 550 million years ago.



To calculate how many million years separate the divergence if eagles and humans from the divergence of rats and mice, compare the time between common ancestors.

Common ancestor of Eagles & Humans was 310 million years ago.

Common ancestor of Rats & Mice was 50 million years ago.

Difference : 310 - 50 = 260

So, the divergence of eagles and humans occurred 260 million years apart from the divergence of rats & mice.

Molecular clocks

DNA sequences can be used as molecular clocks to show **when species diverged** during evolution.

DNA sequences are compared between species. The **more similar the sequences**, the **more closely related** the species are and the **more recently they shared a common ancestor**.

Use of DNA sequences in this way assumes mutation rate remains constant and show differences in DNA sequences or amino acid sequences.

Three Domains of Life

Comparison of DNA sequences has provided evidence of the 3 domains of life:

- **Bacteria**
- **Archaea**
- **Eukaryotes**

The **main sequence of events in EVOLUTION OF LIFE** has also been determined using:

- **Sequence data**
- **Fossil evidence**

This has helped to map out the order in the evolution of life as follows:

Cell

Last Universal Ancestor

Prokaryotes

Photosynthetic organisms

Eukaryotes

Multicellular organisms

Animals

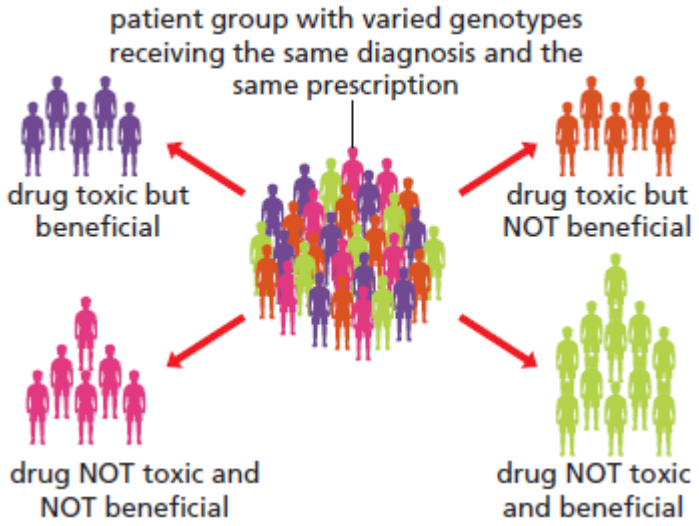
Vertebrates

Land Plants

PHARMACOGENETICS & PERSONALISED MEDICINE

An individual's genome can be analysed to predict the likelihood of developing certain diseases.

Pharmacogenetics is the use of genome information in the **choice of drugs**.



Personalised medicine

An individual's **personal genome sequence** can be used to select the **most effective drugs and dosage to treat their disease.**