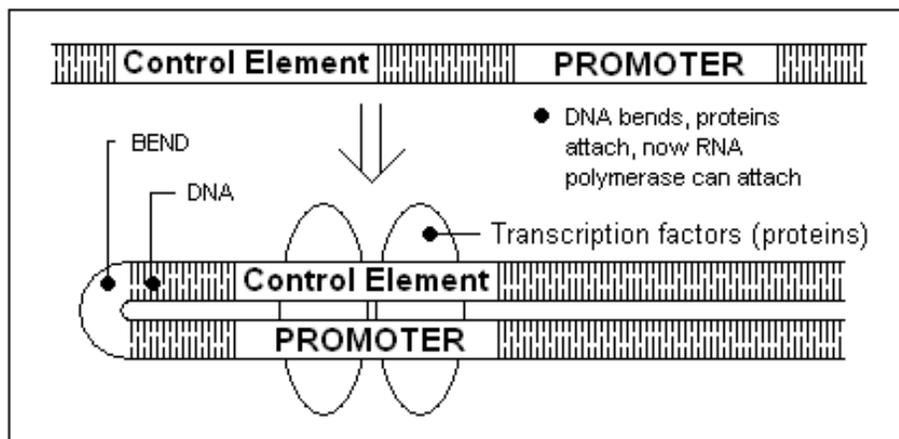


9.7 – Genetics: The Code Broken? (Option)

1. The structure of a gene provides the code for a polypeptide:

- *Describe the processes involved in the transfer of information from DNA through RNA to the production of a sequence of amino acids in a polypeptide:*
 - There are 2 stages in polypeptide synthesis.
 - **STAGE ONE - Transcription:**
 - The 2-stranded DNA in the nucleus untwists for the length of a single gene.
 - One of the strands coding for the gene exposes itself to the nucleoplasm
 - The enzyme, RNA polymerase moves along the strand, attaching loose RNA nucleotides to the DNA, with A-U and C-G, until the whole gene is copied.
 - This new RNA strand is called messenger RNA (mRNA)
 - A start codon, and a stop codon determine the length of the gene
 - **STAGE TWO - Translation:**
 - The mRNA strand binds to a ribosome in the cytoplasm, with the start codon being AUG (always).
 - The ribosome moves along the mRNA strand, to ‘read’ more of its bases.
 - tRNA molecules floating in the cytoplasm, which have anti-codons complementary to the codons of the mRNA enter the ribosome. E.G., if the mRNA had an AAG codon, the UUC tRNA would bind to it
 - The tRNA releases its amino acid to form a polypeptide chain
 - The ribosome can only accommodate 2 tRNA.
 - The ribosome moves along the mRNA, and more and more amino acids are attached, with peptide bonds, to the growing polypeptide chain.
 - When a ‘stop’ codon is reached, the polypeptide chain is released into the cytoplasm, for further processing, to become a protein.
- *Outline the current understanding of gene expression:*
 - A gene is **expressed** when its polypeptide is synthesised, converted to a protein, and the protein is fully functional.
 - Gene Expression – EUCARYOTES:

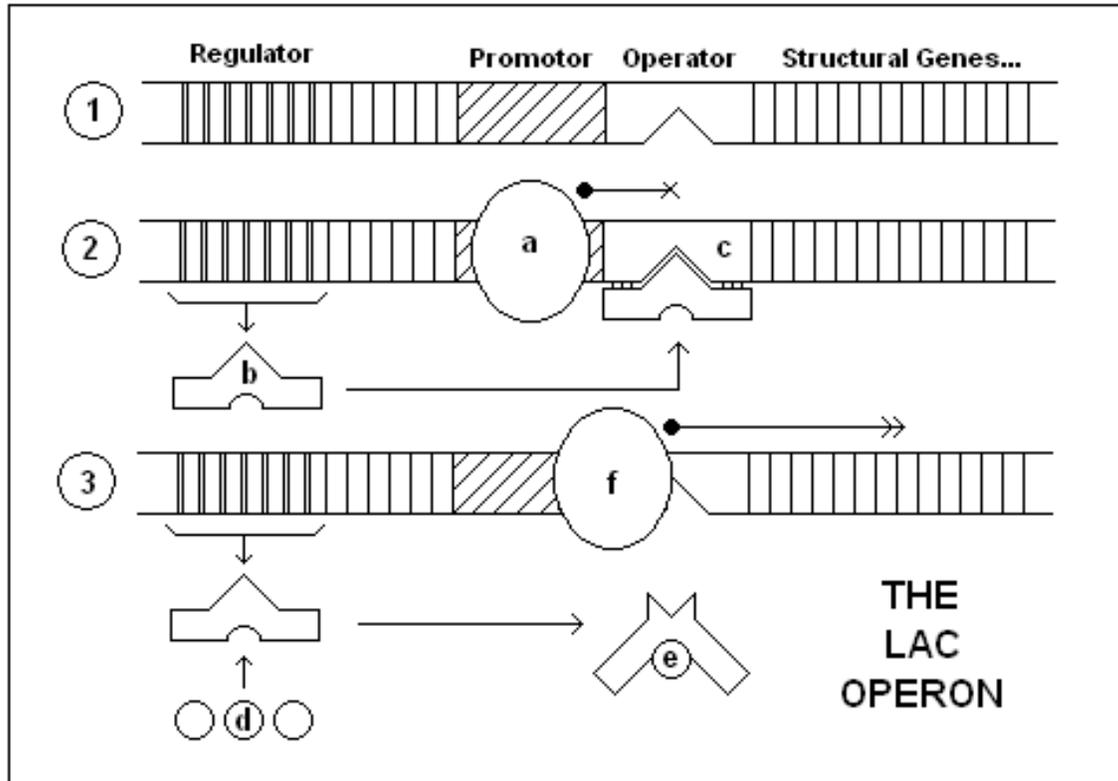
- There are a number of stages that gene expression can be regulated, or stopped, within eucaryotic cells
- Gene expression can be stopped at any of the following stages:
 - **DNA Unpacking:**
 - ◆ In the nucleus, DNA is wound around HISTONE proteins to form a molecular combination called a NUCLEOSOME
 - ◆ Genes that are permanently turned off are packed very tightly
 - ◆ The adding of methyl groups stops gene expression
 - ◆ Adding acetyl groups loosens the DNA from the histones and allows it to be copied more freely, and hence expressed.
 - **DNA Transcription:**
 - ◆ Control of gene expression occurs most commonly in this stage
 - ◆ In a DNA strand, before the gene, there are two sections of nucleotides: firstly there is the control element, then the promoter sequence.
 - ◆ RNA polymerase can only attach to the gene if the DNA strand **BENDS** back over itself and the control element **TOUCHES** the promoter sequence, and proteins called **transcription factors** bind them together.
 - ◆ This combination is called a promoter complex
 - ◆ **ONLY** then can RNA polymerase attach to the gene.



- **Regulation of mRNA:**

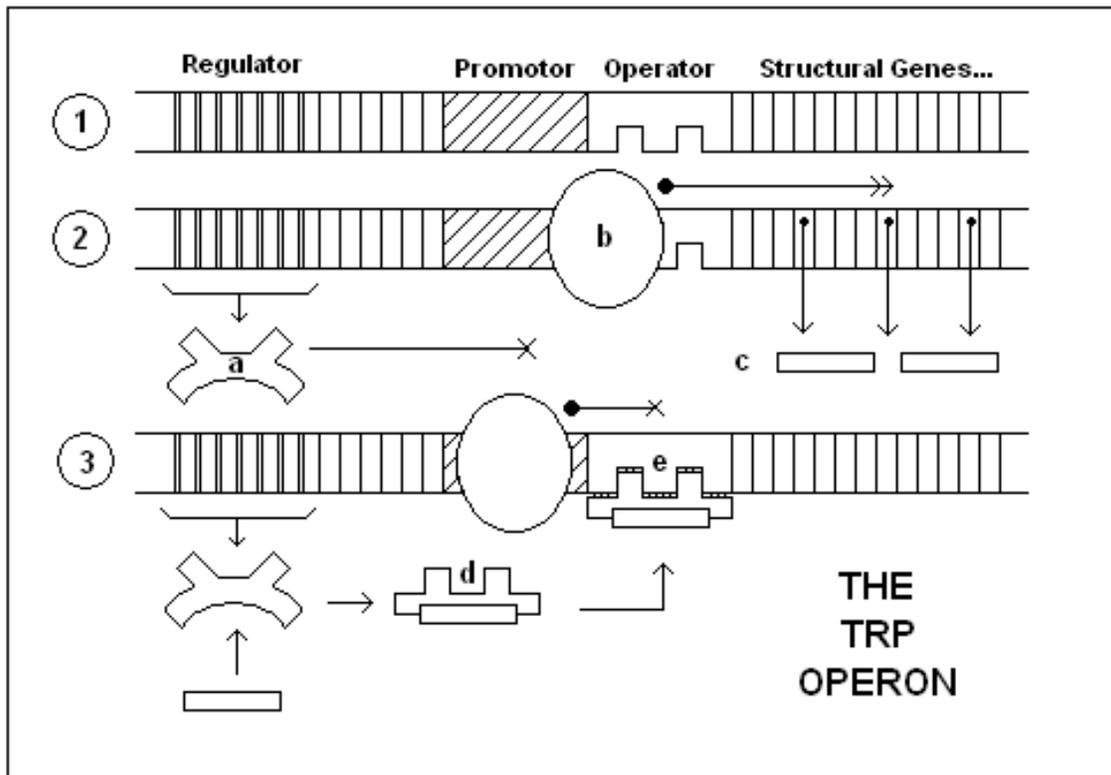
- ◆ The mRNA is first covered with a CAP and a TAIL (made of nucleotides) to protect it from degradation.
- ◆ It then moves out of the nucleus, where it is processed further
- ◆ The non-coding parts (introns) are removed, leaving just the parts that code for proteins (exons)
- **Control of Translation:**
 - ◆ Translation can be blocked by special proteins
 - ◆ These stop the ribosome from moving along the mRNA strand
 - ◆ This prevents the code from being 'read', stopping gene expression
- **Protein Processing and Degradation:**
 - ◆ Polypeptides have to be processed before they can become functional proteins. This involves folding, cleavage or adding non-protein sections. Expression can end if these processes are stopped
 - ◆ Proteins can also be destroyed by proteasomes.
- Gene Expression – PROCARYOTES (Operon Theory):
 - Protein synthesis in procaryotes is controlled by **operons**
 - Operons are sections of the DNA that control the production of mRNA
 - The operons are found ONLY in primitive procaryotes
 - They consist of the:
 - **Regulator Gene:** This is the first section of the operon. It creates proteins that, together with the operator gene, activate or stop protein synthesis
 - Promoter Region:** This section of the operon is the binding site for the RNA polymerase enzyme.
 - **Operator Gene:** This acts with the regulator proteins to control synthesis
 - **Structural Gene(s):** The structural gene contains the information to make the polypeptide (i.e. the functional protein).
 - There are two types of operons:
 - The LAC-Operon
 - The TRP-Operon

- The Lac-Operon:



1. This is an OPERON of DNA with the basic structures for the production of LACTASE – the enzyme for digesting lactose
2. Normally, the RNA polymerase (**a**) attaches to the promoter region. The regulator gene continuously produces the **regulator protein (b)** – this protein travels to the operator gene, where they **bind** together (**c**). This prevents the movement of the RNA polymerase, stopping gene expression. (This is because the enzyme is not needed ALL the time, only when the substrate is present).
3. When the substrate is present, in this case, the lactose molecules (**d**), the process changes. The regulator proteins, which are ALWAYS produced, bind with the lactose molecules (**e**). This binding alters the structure of the regulator protein, so now it is unable to bind to the operator gene. This allows the RNA polymerase to move (**f**), making the enzyme.

- The Trp-Operon:



1. This is the operon showing the basic structures for the production of TRYPTOPHAN – an essential amino acid
2. The regulator gene produces a regulator protein (**a**) called an **inactive repressor**. It is produced to not fit into the operator. This is so the RNA polymerase (**b**) can attach to the promoter and make tryptophan (**c**).
3. When the enough tryptophan has been produced, it will start to build up. When the inactive repressor is produced, the tryptophan will bind to the repressor protein, and alter its molecular shape (**d**). This activates the repressor, so that it can now fit into the operator region and bind to it (**e**). This stops the RNA polymerase from moving, preventing the production of anymore tryptophan.

2. Multiple alleles and polygenic inheritance provide further variability within a trait:

- *Give examples of characteristics determined by multiple alleles in an organism other than humans:*
 - When there are more than 2 alleles (such as brown, blue and green eye colour) for a gene, the characteristic is said to be determined by MULTIPLE ALLELES
 - There may be many forms of the genes (many alleles), but there can only be 2 alleles for each characteristic present in each individual
 - Multiple alleles are likely to arise from *random mutations* of the original form of the gene over a period of time
 - There may be one allele which produces the basic trait called the **wild type**
 - The other alleles are called **mutant** alleles and produce the variations
 - Example: White clover leaf patterns:
 - There are 7 alleles for the patterns on the leaves of the white clover
 - This gives 22 possible phenotypes of leaf pattern for the plant
 - Example: Eye colour in flies:
 - There many different alleles for the fruit fly eye colour, and different combinations of these give different colours, such as red, white, and ‘tinged’
- *Compare the inheritance of the ABO and Rhesus blood groups:*
 - ABO Blood Groups:
 - There are 4 main blood groups in humans: A, B, AB and O
 - These ‘groups’ refer to the presence or absence of two carbohydrates on the surface of the **red blood cells** – the A antigen and the B antigen:

Blood Group	A	B	AB	O
Antigen	Just A	Just B	Both A and B	None

- The knowledge of these different groups is very important when doing blood transfusions – if the blood transfused into an individual has a different substance on the red blood cells, it will be recognised as an **antigen**
- If the wrong type of blood is given, the immune system will cause the blood will clump together (agglutination) and the patient will die:

- AB can accept all blood types – it already has both A and B molecules
- A can only accept A and O blood
- B can only accept B and O blood
- O can only accept O blood (but all can accept O blood)
- **GENETICS** behind ABO groups:
 - The blood group of a person is determined by a single gene
 - This gene has multiple alleles – three alleles in total
 - There is the allele for the A-antigen (symbolised by I^A), the allele for the B-antigen (I^B) and the allele for no antigen (I^O)
 - **Genetic relationships:** I^O is recessive to both I^A and I^B , and I^A is codominant with I^B .

Blood Group	A	B	AB	O
Genotype	$I^A I^A$ or $I^A I^O$	$I^B I^B$ or $I^B I^O$	Only $I^A I^B$	Only $I^O I^O$

- Rhesus Blood Groups:
 - In addition to the A and B antigens on the surface of the red blood cells, there is also another substance, called the **Rhesus factor**
 - This substance is controlled by a different gene
 - The Rhesus factor is either present or absent on the cell
 - EG – A person with blood type A^+ has the A antigen AND the Rhesus factor, while a person with B^- has the B antigen but no Rhesus factor
 - **GENETICS** behind the Rhesus factor:
 - There are 2 alleles, the allele for making the antigen (Rh^+) and the allele for not making the antigen (Rh^-)
 - The Rh^+ allele is dominant over the Rh^- allele
 - With the Rhesus factor – genotype either Rh^+Rh^+ or Rh^+Rh^-
 - No Rhesus factor – genotype Rh^-Rh^-
- Comparing Forms of Inheritance:
 - **Similarities:** Both characteristics are determined by a single gene; there is simple dominance present
 - **Differences:** ABO is has multiple alleles, Rhesus only has 2; there is codominance in ABO; ABO has 3 phenotypes, Rhesus only has 2.

- *Define what is meant by polygenic inheritance and describe one example of polygenic inheritance in humans or another organism:*
 - **Polygenic inheritance** is when a particular characteristic is determined by more than one gene
 - Characteristics that are determined by multiple genes show continuous variation – this means that members of the same species show a *wide range in variation* for this particular characteristic
 - The greater the number of genes that determine the characteristic, the more variation there will be
 - Most human characteristics are polygenic:
 - EG: Height:
 - This trait in humans is determined by many genes
 - It is identified as polygenic inheritance because individuals in the human population do not fall into discrete height groups (such as ‘tall people’ and ‘short people’) but rather form a continuous series of variations in height
- *Outline the use of highly variable genes for DNA fingerprinting of forensic samples, for paternity testing and for determining the pedigree of animals:*
 - All organisms produced by sexual reproduction have unique DNA and every body cell comes with a set of this DNA
 - Although it is the coding regions of DNA (exons) that produce the individual proteins that make up an organism, it is the non-coding sections of DNA (introns) that scientists used to uniquely genetically identify an individual
 - This process is called DNA fingerprinting
 - The non-coding sections of the DNA consists of lengths of base sequences that are often **repeated many times**
 - The sections are called ‘micro-satellites’ (or short tandem repeats)
 - Organisms inherit half of their non-coding sequences from their mother and half from their father, to give a unique pattern of non-coding DNA sequences
 - Recombinant DNA technology enables the analysis of the DNA of an organism
 - Scientists use about 10 known DNA regions to create a DNA profile of DNA fingerprint of an individual

- This can then be compared to other samples for various uses
- Uses of DNA profiling:
 - **Forensic Investigations:** Forensic science uses DNA fingerprinting to compare the DNA found in samples of blood, saliva or other body tissue found at a crime scene with that of suspects. The evidence is admissible in courts.
 - **Paternity Testing:** Paternity testing in humans relies on the analysis of the DNA of the child and the father, and comparing them to determine lineage. Cells from the skin, blood or other tissue are used
 - **Animal Pedigrees:** DNA profiling is mainly used to show parentage in animals. Breeders of animals such as sheep and cattle need to know the parents of the offspring – they want to preserve desirable characteristics.
- Benefits of DNA Fingerprinting:
 - DNA is more accurate than previous methods of identification, such as the ABO blood groups. The chances of two individuals having the same DNA profile is almost impossible
 - Only a tiny sample of DNA is needed to obtain results. DNA can be multiplied using a process called a ‘polymerase chain reaction’
- Summary of DNA Fingerprinting Procedure:
 - First, DNA is cut into fragments using **restriction enzymes**
 - **Gel electrophoresis** is used to separate the fragments of DNA by weight – an electric field is used to make the fragments move within a gel. Smaller fragments move further away
 - **Southern blotting** methods transfers the DNA fragments from gel to paper
 - **DNA hybridisation** methods are used to bind radioactive probes to the fragments of DNA
 - **Autoradiography** – paper is overlaid with photographic paper. The probes that bound to the DNA were radioactive and so show up on the photo paper as dark bands.
- *Process information from secondary sources to identify and describe one example of polygenic inheritance:*

– The Colour of Wheat Kernels:

- There are 2 genes that determine this particular trait
- They control the redness or whiteness of the wheat kernels
- Each gene has only two alleles, and they exhibit a simple dominant-recessive relationship – dark is always dominant to light
- For the first gene, the two alleles are R_1 (dark red) and r_1 (white)
- Likewise the alleles of the second gene are R_2 (dark red) and r_2 (white)
- The phenotypes and genotypes are:

Genotype	Phenotype
$R_1R_1-R_2R_2$	Dark red kernels
$R_1R_1-R_2r_2$ $R_1r_1-R_2R_2$	Medium-dark red kernels
$R_1r_1-R_2r_2$ $R_1R_1-r_2r_2$ $r_1r_1-R_2R_2$	Medium red kernels
$R_1r_1-r_2r_2$ $r_1r_1-R_2r_2$	Light red kernels
$r_1r_1-r_2r_2$	White kernels

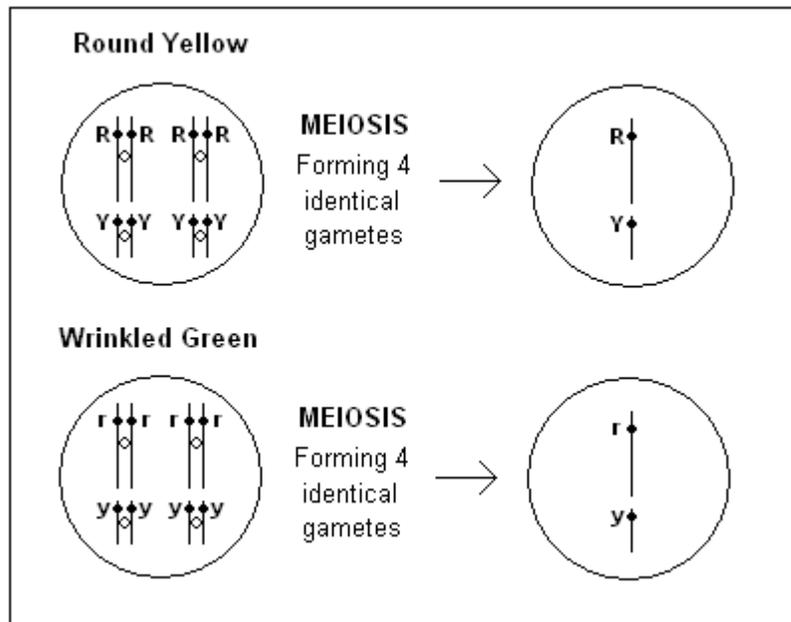
3. Studies of offspring reflect the inheritance of genes on different chromosomes and genes on the same chromosomes:

- Use the terms 'diploid' and 'haploid' to describe somatic and gametic cells:
 - SOMATIC cells are the body cells
 - GAMETIC cells are the sex cells
 - Somatic cells are **diploid** cells, that is:
 - Chromosomes are in pairs
 - There are 2 sets of chromosome – 2N number of chromosomes
 - Gametic cells are **haploid** cells, that is:
 - Chromosomes are single
 - There is 1 set of chromosomes – N number of chromosomes
- Describe outcomes of dihybrid crosses involving simple dominance using Mendel's explanations:
 - Previously, we looked at **monohybrid** crosses, where only one characteristic was examined at a time (eg - pea colour)
 - Mendel also performed **dihybrid** crosses, where two characteristics were examined at a time
 - This was one of the crosses he performed:
 - He knew ROUND (R) seeds were dominant to WRINKLED (r) seeds
 - He knew YELLOW (Y) seeds were dominant to GREEN (y) seeds
 - Mendel crossed two pure-breeding plants that had the phenotypes of **round-yellow** and **wrinkled-green**. The following results were obtained:

Parents	Round Yellow × Wrinkled Green
F₁ Generation	100% Round Yellow
<i>Mendel then interbred the F₁ individuals</i>	
F₂ Generation	9 Round Yellow: 3 Round Green: 3 Wrinkled Yellow: 1 Wrinkled green

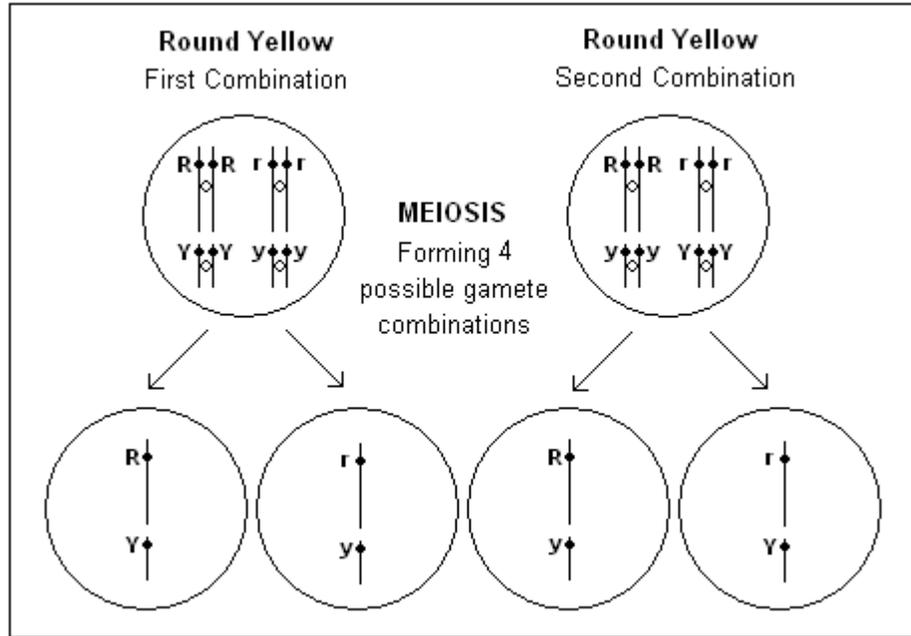
- This special ratio of 9:3:3:1 is called the dihybrid ratio
- **Significance of Results:**
 - However, looking at each trait separately, the ratio of round-wrinkled as well as the ratio of green-yellow is still 3:1 (after simplification).

- This means the two features had behaved **INDEPENDENTLY** of each other – taking 2 traits at a time didn't affect the results of each trait
 - This is Mendel's Second Law – The law of independent assortment:
 - Each pair of factors can combine with either of another pair of factors
 - In modern terms – during fertilisation, either allele of the gene pair can combine with either allele of another gene pair.
- Genetic explanation of the **DIHYBRID CROSS**:
- **THE FIRST CROSS (Pure-Breeding Parents):**
 - **Phenotype:** Round Yellow × Wrinkled Green
 - **Genotype:** RRYT × rryy
 - Results of Meiosis:
 - ◆ Since the parent cell is **HOMOZYGOUS**, only one type of gamete can be formed (RY) – see diagram:



- **Possible Gametes:** RY × ry
- **Result of Cross – F₁ Generation:**
 - ◆ All offspring are RrYy (looking at gametes, this is the only possible combination for offspring.)
 - ◆ Phenotype 100% - Round Yellow (just like Mendel's results)
- **THE SECOND CROSS (Interbreeding Heterozygous F₁ Generation):**

- **Phenotype:** Round Yellow × Round Yellow
- **Genotype:** RrYy × RrYy
- Results of Meiosis:
 - ◆ The cells undergoing meiosis are **HETEROZYGOUS** – there are two alleles present. The process of **independent assortment** (also called random segregation) can produce variations in gametes:



- ◆ Each cell that is heterozygous for both traits can produce 4 possible gametes – this explains Mendel’s second law

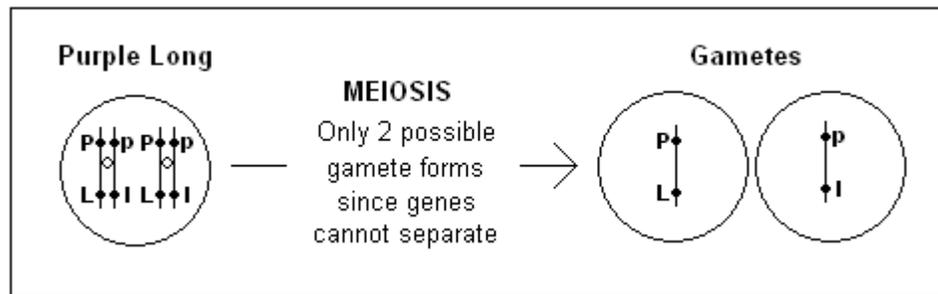
- **Possible Gametes:** RY, Ry, rY, ry × RY, Ry, rY, ry

×	RY	Ry	rY	ry
RY	RRYY	RRYy	RrYY	RrYy
Ry	RRYy	RRyy	RrYy	Rryy
rY	RrYY	RrYy	rrYY	rrYy
ry	RrYy	Rryy	rrYy	rryy

- **Results:**
 - ◆ RRYY: 2 RRYy: RRyy: 2 RrYY: 4 RrYy: 2 Rryy: rrYY: 2 rrYy: rryy
 - ◆ In terms of phenotype this is:

9 Round Yellow	3 Round Green	3 Wrinkled Yellow	1 Wrinkled Green
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- *Predict the difference in inheritance patterns if two genes are linked:*
 - Two genes are said to be **linked** if they are on the same chromosome
 - Looking at the pea plant example above, it can be seen that the two characteristics chosen were on different chromosomes.
 - During meiosis, linked genes remain together in normal circumstances
 - Therefore linked genes do NOT follow Mendel’s genetics laws.
 - Example: In pea plants, flower colour and pollen shape are linked traits. Purple (P) is dominant to red (p) flower and long-pollen (L) is dominant to round pollen (l):
 - THE FIRST CROSS (Homozygous parents):
 - **Phenotype:** Purple-Long × Red-Round
 - **Genotype:** PPLL × ppll
 - **Gametes:** PL × pl
 - **Results:** All PpLl (Purple-Long)
 - ◆ This result is no different to unlinked genes
 - THE SECOND CROSS (Interbreeding F₁ Generation):
 - **Phenotype:** Purple-Long × Purple-Long
 - **Genotype:** PpLl × PpLl
 - ◆ The formation of gametes is where linked genes start to get different:

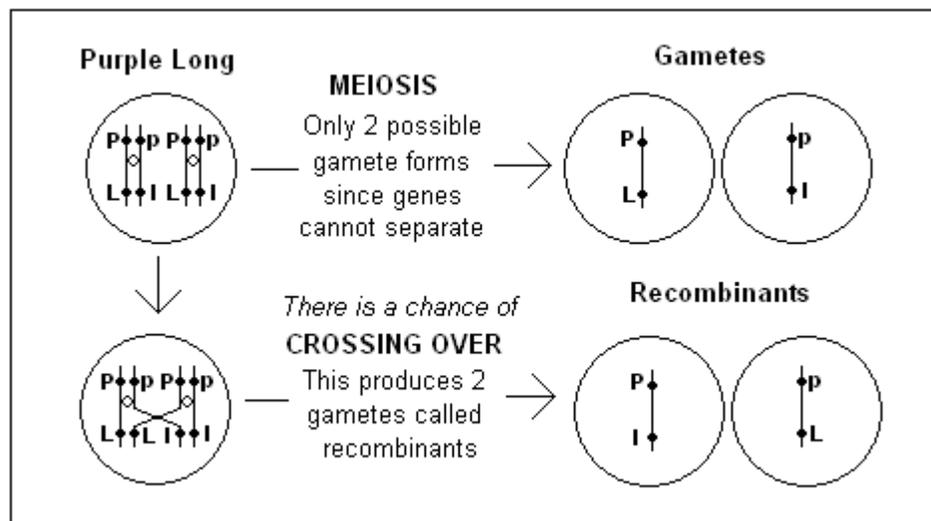


➤ **Gametes:** pl, PL × pl, PL

×	PL	pl
PL	PPLL	PpLl
pl	PpLl	ppll

- So the **expected** result would not be the 9:3:3:1 ratio, but it is a 3:1 ratio
- **HOWEVER** – This expected result often doesn’t happen

- *Explain how cross-breeding experiments can identify the relative position of linked genes:*
 - When the ACTUAL dihybrid cross is performed (of the flower colour and pollen shape), the results are a bit different
 - In a sample of 100 offspring, the actual results are:
 - Purple flowers, long pollen: **68**
 - Red flowers, short pollen: **18**
 - Purple flowers, short pollen: **7**
 - Red flowers, long pollen: **7**
 - Looking above at the Punnett square, the result does not predict the existence of the purple-short and red-long combinations
 - These are formed by CROSSING-OVER (which happens in Prophase 1)
 - Above, we only predicted the two gametes **pl** and **PL**.
 - Crossing-over produces the two new gametes **Pi** and **pL** – these new gametes are called recombinant gametes – the offspring are called RECOMBINANTS



- The amount of crossing over is not the same for every pair of genes
- The DEGREE of crossing over is determined by the DISTANCE between the two genes on the same chromosome:
 - The smaller the distance between the two genes on the chromosome, the less likely crossing over will occur, and the less recombinants there will be.

- Using this important fact, the **relative distance** between genes on a chromosome can be determined by looking at percentage of offspring that are recombinants.
- This is also called the CROSSOVER FREQUENCY
- Example: Using the same results above:
 - In a sample of 100 offspring, the actual results are:
 - Purple flowers, long pollen: **68**
 - Red flowers, short pollen: **18**
 - Purple flowers, short pollen: **7**
 - Red flowers, long pollen: **7**
 - Looking at the results, there are 14 recombinants, with 100 offspring in total
 - So the percentage of recombinants, or crossover frequency is 14
 - This means that the **flower colour gene** is 14 UNITS apart from the **pollen shape gene** on the same chromosome
 - This information can be used to make a chromosome map, which shows the relative position of all genes
- *Discuss the role of chromosome mapping in identifying relationships between species:*
 - Organisms of the same species have the same chromosome maps
 - **Linkage groups** are groups of linked genes
 - If linkage groups can be found in different organisms, it can be used as a method of analysing the relationships between species
 - Evidence of similarities in linkage groups between species suggests that in the past they shared a common ancestor.
 - Together with traditional selective breeding techniques and new DNA sequencing technologies, chromosome mapping helps identify relationships between species.
 - These all provide another source of evidence for the evolution of living organisms.

4. The Human Genome Project is attempting to identify the position of genes on chromosomes through whole genome sequencing:

- *Discuss the benefits of the Human Genome Project:*
 - **The Human Genome Project:**
 - A *genome* is the complete set of genetic material of an organism.
 - The Human Genome Project involves determining the position of every gene in each of the chromosomes.
 - It will also determine the base sequence of every gene
 - **The Benefits of the HGP:**
 - Greater Understanding of Genetics:
 - Scientists will be able to explain more clearly how genes are expressed and how genes are inherited
 - The results of gene mutation will be better known
 - It will explain how genes interact with each other
 - Some genes' function are still unknown; knowledge of the human genome may help to unravel the functions of these genes.
 - Understanding of Human Evolution:
 - The genomes of other species can be compared with the human genome
 - This will give insights into the similarities or differences in the pathways of evolution between humans and other species
 - Detection of Disease and Improvement in Human Health:
 - Faulty genes which cause disease can be detected before the disease can develop
 - This can lead to new diagnostic tests and the possibility of genetic counselling for individuals who are carriers of faulty genes.
 - Normal genes may be cloned and the products of these genes can be used to treat disease in other individuals (e.g. insulin for diabetics)
 - The new technology of gene therapy is possible because of the Human Genome Project – it involves administration of a gene to an individual who has a defective copy of it

- *Describe and explain limitations of data obtained from the Human Genome Project:*
 - Knowing the base sequence of genes does not provide knowledge about the function of the **proteins** produced – “DNA to RNA to Proteins” is a simplification.
 - A lot of the DNA is non-coding (introns) – probably useless “junk DNA”
 - Knowing the entire base sequence of the human DNA does not explain all the biochemistry and functioning of human beings
 - There has been criticism of the huge amounts of money being spent of the HGP – the value of the results, compared the to same amount of money spent on other projects, has been criticised.
 - Ethical Problems: The problems of who has access to information, what it can be used for, whether or not it can be used for financial gain, or the possibility of people being singled out with “inferior genes”, etc. is still being hotly debated.
- *Outline the procedure to produce recombinant DNA:*
 - Firstly, the gene to be extracted needs to be identified
 - Special enzymes (restriction enzymes) are used to cut the gene out from the DNA
 - A circular ring of DNA found in bacteria, called a PLASMID is also cut using the same enzymes
 - The genes and the plasmid are mixed together, and the matching ends join loosely
 - Chemicals called DNA ligases act as a “glue” and stick them together (annealing)
 - This is the recombinant DNA – it can either be used to create the protein, or cloned to produce more of the specific gene.
- *Explain how the use of recombinant DNA technology can identify the position of a gene on a chromosome:*
 - The position of genes on a chromosome are located using fluorescent DNA probes, and DNA hybridisation technology:
 - Firstly, the dividing cells are placed on a microscope slide – whole chromosomes are visible under the microscope during division
 - Using heat, the DNA strands are denatured – the strands separate into single strands

- Fluorescent probes are synthetic strands of DNA that are produced to be complementary to known genes. Also, a fluorescent tag is also added so that the location of the gene will be known.
 - The probes are added to the slide of the denatured DNA strands
 - Since the strands are single stranded, and the probes are single strands, the probes will attach to the DNA where the bases are complementary.
 - Looking under the microscope, the location of the gene can be clearly seen.
- *Assess the reasons why the Human Genome Project could not be achieved by studying linkage maps:*
 - Linkage maps show just the **order of genes** on a chromosome, and their relative distance apart (remember “cross-over frequency”)
 - The Human Genome Project sought to find the exact positions (not relative positions) of genes on a chromosome, and therefore could not be achieved by studying linkage maps alone.
 - Also, linkage maps for organisms such as *Drosophila* have been produced by studying recombination frequencies gained from breeding experiments.
 - Because carrying out human breeding experiments are unethical and impractical, data could not be obtained in this way.
 - Linkage maps give information based on parts of the genome that get expressed – that is, the exons that make proteins that make our features.
 - Since most of the genome is non-coding, these non-coding regions wouldn't be identified by linkage maps
 - Linkage maps do not identify the nucleotide base sequence, like the HGP did.

5. Gene therapy is possible once the genes responsible for harmful conditions are identified:

- *Describe the use of gene therapy for an identified disease:*
 - GENE THERAPY is the process by which techniques are developed to replace defective genes with normal genes.
 - It works by extracting healthy genes from healthy cells and inserting them into the diseased cells, usually through the use of a viral vector
 - Gene therapy is currently being trialled to cure the genetic disease **cystic fibrosis**
- *Identify a current use of gene therapy to manage a genetic disease, a named form of cancer or AIDS*
 - **Gene Therapy and Cystic Fibrosis:**
 - Cystic Fibrosis is a genetic disease that is caused by a defective recessive gene
 - The presence of 2 of the recessive alleles results in the lack of production of a protein that is part of the cell membrane – it affects the transport of ions across the membrane
 - One of the most obvious symptoms is an excess of thick mucus in the lungs, which causes respiratory damage, leaving a life expectancy of 30 years
 - The gene therapy procedure replaces the defective gene with a healthy gene in the somatic (body) cells of the individual
 - This is called SOMATIC GENE THERAPY
 - The process:
 - A virus, called the AVV virus, is a harmless virus that is found in many healthy humans. It is used as a vector in gene therapy as it has the ability to insert its DNA into the DNA of the host cell
 - Using recombinant DNA technology, the healthy gene is inserted into the genome of the AVV virus.
 - A tube is placed through the nose of the affected patient, into the lungs, and the virus is dripped into the lungs.
 - This gene therapy is slow, and relies on the gradual replacement of the defective genes with healthy ones

- It has not yet been successful in curing the disease, as treatment is still in early stages of development, and the treatment itself is quite slow
- Also, the body's natural response to the virus can affect its effectiveness
- Inflammation of the lungs and general discomfort are some of the current side-effects of this form of somatic gene therapy

6. Mechanisms of genetic change:

- *Distinguish between mutations of chromosomes, including rearrangements, changes in chromosome number, including trisomy, and polyploidy, and mutations of genes, including base substitution and frameshift:*
 - Chromosome Mutations:
 - Mutations involving whole chromosomes can be either:
 - A change in the number of chromosomes
 - A change in the arrangement of genes on the chromosome
 - **Changes in Chromosome Number:**
 - This is due to the NON-DISJUNCTION of chromosomes during meiosis – that is, when the chromosomes line up in the centre of the cell in pairs, but fail to separate to the two sides of the cell
 - This results in mutant gametes – some contain fewer chromosomes, while others contain extra chromosomes
 - **E.g. DOWN'S SYNDROME:** Is a result of non-disjunction of the 21st chromosome (C-21). When the gametes are produced, one of them has two of C-21, while the other is completely missing the chromosome (gametes usually have only one chromosome). When a double chromosome gamete fuses with a normal, single chromosome gamete, the resulting individual has 3 copies of the chromosome.
 - Having 3 homologous chromosomes is called TRISOMY
 - In Down's Syndrome it is just trisomy-21, but if a mutant diploid gamete (2n) fuses with a normal haploid gamete (n), a triploid will occur (3n).
 - This is called POLYPLOIDY: The occurrence of whole extra sets of chromosomes in an individual.
 - Polyploidy is usually fatal in humans, and other animals, but is actually very common in plants
 - In some cases, polyploidy is advantageous in plants – polyploid plants can grow faster and larger, and produce bigger fruit.
 - **Changes in Arrangement of Genes on Chromosomes:**
 - These mutations occur during the CROSSING-OVER stage in meiosis

- The mutations occur when chromosomes break and reform, but are altered in the process
 - There are 4 types of gene rearrangement: they are deletion, replication, translocation and inversion
 - Deletion: This is when part of a chromosome is lost or destroyed. All the genes in that section are also destroyed. E.G. **Cri-du-chat Syndrome**
 - Duplication: This is when a section of the chromosome is copied and added on; extra genes means excess proteins are made. Often lethal.
 - Translocation: This is when a section of a chromosome breaks off, but reattaches to another chromosome. E.G. **Translocation Down Syndrome**
 - Inversion: In this mutation, a section of the chromosome breaks off, flips, and reattaches to the same chromosome, but backwards.
- Gene (Point) Mutations:
- **Base Substitution**: The most common gene mutation
 - Occurs when one base in the DNA sequence is substituted for another
 - Hence only one codon is altered and only one amino acid is altered (but since multiple codons can code for one amino acid, these can be harmless)
 - The change of just one amino acid in a protein can be very harmful
 - E.G. Sickle-Cell Anaemia: A single point mutation causes this disease. In the gene, one thymine base is replaced with an adenine base. This results in glutamic acid being replaced with valine, and as a result, the haemoglobin in the red-blood cells are malformed and cannot carry as much oxygen as normal.
 - **Frameshift Mutation**:
 - Occurs when a base is added or replaced from the DNA strand.
 - This is potentially a highly damaging mutation, as the entire base sequence is shifted from the one point and onwards.
 - The impact of frameshift mutations compared to point mutations is much greater as the code for all the amino acids for the gene is changed.
 - E.G. Muscular Dystrophy: The body's gene to produce a protein in muscles, called dystrophin, is mutated by frameshift.

- *Outline the ability of DNA to repair itself:*
 - Cells contain natural DNA repair mechanisms
 - Copying errors can be repaired by enzymes such as DNA polymerase
 - The **DNA repair enzyme** uses the undamaged strand of DNA as a template to replace the base sequence in the damaged strand of DNA
 - Nucleotide excision repair involves recognition of damage, cutting of the DNA strand and replacing the bases and repairing the bonds.
- *Describe the way in which transposable genetic elements operate and discuss their impact on the genome:*
 - Transposable genetic elements, (or **transposons**) are discrete sections of DNA that can move around among chromosomes – “Jumping Genes”
 - Impact on the Genome:
 - They can transfer a gene or groups of genes to a structurally unrelated part of the DNA (or even another chromosome)
 - This creates new nucleotide sequences and chromosomal rearrangement
 - These jumping-genes, like in bacteria, can transfer DNA from one cell to another. This explains the rapid spread of antibiotic resistance in certain strains of bacteria.
 - Transposons are also thought to have a role of gene expression, though this function is not fully understood.
- *Distinguish between germ-line and somatic mutations in terms of their effect on species:*
 - GERM-LINE cells produce **gametes**
 - Hence, a mutation in the germ-line cells can be passed on to the next generation
 - The offspring of the individual with the germ-line mutation carry the mutation
 - Thus, the mutation becomes part of the gene-pool of the species, affects the population, and increases the chance of evolution
 - SOMATIC cells are **body cells**
 - Somatic mutations are usually a result environmental factors (eg radiation)
 - These mutations cannot be passed onto offspring, and do not affect the gene pool

- *Describe the effect of one named and described genetic mutation on human health:*
 - **Disease:** Down's Syndrome
 - **Cause:** Trisomy 21, due to disjunction of the chromosomes during meiosis
 - **Effects:** Lower than average mental ability, almond shaped eyes, shorter limbs, speech impairment, enlarged tongue and a high risk of heart failure. Children with Down syndrome will need special care in many areas of life, including eating, washing and general hygiene. The reduced mental capacity, a symptom of the disease, may be a limiting factor on the development on the individual in respect to social development, schooling and the workforce. An important issue is the physical health of the patient with the disorder. Physiotherapy may be needed, as children born with Down syndrome have weakened muscles, and shorter arms and legs. The increased risk of several diseases, most notably cardiovascular failure, is an important issue that must be managed with Down syndrome patients.

7. Selective breeding is different to gene cloning but both processes may change the genetic nature of species:

- *Explain, using an appropriate example from agriculture, why selective breeding has been practised:*
 - Selective breeding is the practise of selecting animals with characteristics that benefit humans, and breeding them.
 - Selective breeding is practised so that plants or animals that have characteristics that are favourable to humans become more common, and can benefit humans.
 - It involves choosing animals with a particularly highly prized characteristic and breeding them so the characteristic is passed on to the next generation
 - **E.G. Cows and Milk Production:**
 - Originally, 2 breeds of cows were used to produce milk – the Friesian cows produce ‘lots of milk’, while the Jersey cows produce ‘creamy milk’, both of which are beneficial to humans
 - By cross-breeding the two cows, both characteristics were combined into a hybrid cow that produced ‘lots of creamy milk’
 - Selective breeding can actually change the genetic nature of a species’ population quite dramatically.
- *Describe what is meant by ‘gene cloning’ and give examples of the uses of gene cloning:*
 - Gene cloning is the process of making multiple copies of a **single gene**
 - **Producing Gene Clones:**
 - Recombinant DNA technologies are the main technique used
 - Genes or DNA fragments are often extracted from the donor, and then inserted into bacterial plasmids, which then reproduce rapidly – many clones produced
 - A new technology developed is the PCR (polymerase chain reaction)
 - It is the fastest method for gene cloning – it is an artificial process that replicates the gene many times without cells
 - **Uses of Gene Cloning:**
 - Producing multiple copies of a gene for analysis (eg, forensics)

- Producing useful protein products such as human growth hormone, or insulin
 - Producing human interferon used to require litres of human blood, but is now produced by gene cloning
 - Producing genes for gene therapy
 - For making transgenic organisms
- Distinguish between gene cloning and whole organism cloning in terms of the processes and products:

	Gene Cloning	Whole Organism Cloning
Products	Multiple copies of a <u>single gene</u> are produced. The produced gene is identical to the original gene that was used.	Whole genetically identical <u>organisms</u> are produced. Total genetic make-up identical to original organism.
Processes Used	Only a section of DNA is extracted. Multiple copies of the gene are made by insertion into a bacterium, or by a polymerase chain reaction	ANIMAL clones – derived from one cell, using nuclear transfer technology. PLANT clones – a single cell can be used. Tissue culture technology.
Reasons for Use	The purpose is to <u>transfer</u> genes from one organism to another. Genetic make-up of the new organism is changed.	The purpose is to produce genetically identical individuals from a single individual
No. of Products	Very large quantities of genes.	Only a few organisms produced.

- *Discuss a use of cloning in animals or plants that has possible benefits to humans:*
 - Production of beneficial human proteins, such as insulin or interferon, involves the cloning of human genes and the insertion of these genes into bacteria
 - Production of crops with a longer shelf life, such as frost-resistant tomatoes, etc, also involves extracting genes, cloning them and inserting them into different species
 - Whole organism cloning may have benefits such as the production of hearts, lungs, or other organs that can be transplanted in the case of disease, with a certainty of no rejection.
 - Plant cloning is also used to reproduce favourable characteristics – cloning with plants however involves tissue culture and cutting and grafting techniques.

- *Trace the history of selective breeding of one species for agricultural purposes and use available evidence to describe the series of changes that have occurred in the species as a result of this selective breeding:*
 - The History of Wheat Breeding:
 - It is the first cultivated crop in the history of humankind
 - Wild wheat grasses were grown 10000 years ago in Ancient Mesopotamia
 - The crop reached Europe, Asian and North Africa around 3000 years ago
 - New breeds formed when domesticated wheat were fertilised by pollen from wild grasses
 - Farmers would select the best wheat strains replant them in the next cycle
 - 1788:
 - Wheat was farmed in Australia, but would only grow in areas with abundant rainfall and favourable soil
 - Therefore because of Australia's poor soil and no guarantee of rainfall there was often insufficient crop yield
 - Diseases such as stem rust would further destroy the crops
 - 1889:
 - William Farrer began a wheat breeding program using varieties from all over the world
 - The characteristics he sought to breed were rust resistance, early ripening and good bread-making properties (high gluten levels)
 - Wheat strains from India gave the best early ripening characteristics and also had short stems and more grains per wheat stalk.
 - Farrer released his 'Federation Wheat' in 1902, which matured early and escaped rust-damage and had high yield.
 - Soon, most wheat grown in Australia was Federation Wheat, and it was able to withstand the dry climate and harsh heat of Australia.
- *Describe the processes used in the cloning of an animal and analyse the methodology to identify ways in which scientists could verify that the produced animal was a clone:*

- **Nuclear Transfer Technology:**
 - DNA from the animal to be cloned is removed from a somatic (body) cell
 - An embryo is extracted from a donor, and the haploid genetic information is removed
 - The DNA is then inserted into the empty embryo, and a light electric shock is used to fuse the DNA into the embryo
 - Another electric shock is used to stimulate cell division, and the mass of cells that is produced (zygote) is inserted into the uterus of another animal.
 - The animal that is born after the gestation period is a clone of the animal the original DNA was extracted from.
- **Embryo Splitting:**
 - When an embryo first starts to divide, zygote is a mass of identical cells
 - The embryo is removed, and the cells are split
 - Each cell is then cultured individually, and the resulting organisms are all clones – all genetically identical.
- Methods to Identify the Organism is a Clone:
 - A method that can verify that it is a clone is DNA hybridisation
 - DNA from both organisms is extracted
 - Using heat, the hydrogen bonds can be broken, and the DNA separates into single strands.
 - The single strands are mixed together, and since the organisms are clones, the single strands will match up completely, with no non-complementary sections.

8. The timing of gene expression is important in the developmental process:

- *Identify the role of genes in embryonic development:*
 - During the development of the embryo, different cell types are produced in a precise pattern in space and time
 - The differences in cells of the embryo results from the expression of different genes – certain genes are switched on or off during development
 - The genes that are turned on during embryonic development are influenced by the POSITION of the cells in the embryo
 - Chemicals which diffuse into the cells alter gene expression.
 - A variety of proteins called **activators** and **repressors** combine with different parts of the DNA causing interactions between various proteins and genes. As a result, some are expressed and others are inhibited.
 - HOX genes (described later) also play an important part in controlling the development of body shape, structure and organisation of an organism.
- *Summarise the role of gene cascades in determining limb formation in birds and mammals:*
 - **Homeobox genes** (HOX genes) are MASTER genes that produce proteins that activate or suppress the expression of the large number of genes in the formation of various body structures (such as limbs)
 - The homeobox genes start the GENE CASCADE – that is they produce the proteins that start a “chain reaction” to induce the development of body structures in the right places of the organism.
 - Homeobox genes direct the development of segments in the embryo, starting from the front, and eventually reaching the back (develops in a sequence)
 - In the case of development of **limbs**, the gene cascade turns on the genes for limbs in specific sections, stimulating the development of limb buds
 - Within these limb buds, a further gene cascade occurs that stimulates that development of cells in the correct pattern of bone, muscle and tissue. Similarly to how the homeobox genes work from the front of the organism to the back, the limbs develop from the base of the “bud” to the extremities – fingers, etc.
 - HOX 9-13 control limb development in birds and mammals

- *Describe the evidence which indicates the presence of ancestral vertebrate gene homologues in lower animal classes:*
 - Gene homologues are DNA sequences that are similar in many different species
 - In the *Drosophila* fruit fly, 8 genes were identified that controlled structural development of the body of the fly.
 - The physical order of the HOX genes on the chromosome matched the physical order of the body segments of the fly (i.e. the gene controlling the position of the head comes before the gene for the thorax, which is before the gene for the abdomen, etc.)
 - Also, when the genes were intentionally mutated, severed structural mutations occurred, such as legs growing out of the fly's head.
 - Using DNA probes that were complementary to the homeobox genes, it was found that the same gene was found in a large range of animals, such as worms, insects, cats, cows and also humans.
 - In vertebrates, the number of HOX genes is greater than in invertebrates.
 - Invertebrates have HOX genes on only one chromosome, while vertebrates have them on 4 chromosomes; HOX A, B, C and D.
 - When the HOX genes from both the insects and the mammals were compared, the following observations were made:
 - In both, the physical order of the genes along the chromosome corresponded to the spatial (physical) order of the structure they coded for along the head to tail axis of the embryo
 - The base sequence of HOX genes are similar in insects and in mammals.
 - If the gene was transferred from insect to mammal, or vice versa, it would do the same job.
 - Therefore, the gene was probably inherited from a common ancestor of both vertebrates and invertebrates
 - The vertebrates have extra HOX genes possibly due to chromosome duplication or polyploidy along the course of evolution
 - Since they have survived a long time without change, they must be very significant.

- *Discuss evidence available from current research about the evolution of genes and their actions:*
 - Recent studies have shown the presence of homeobox genes in most groups of multicellular animals.
 - This implies that the genes evolved in an ancestor common to all animals
 - When comparing the HOX genes of flies and mammals, not only are they similar in structure, but they also have similar functions.
 - DNA sequencing has also revealed an evolutionary progression in the change of DNA of some genes.
 - **E.G.** The genes that code for haemoglobin proteins. Studies of DNA sequences that code for the globin proteins has produced the variety of haemoglobin present in different mammals today. These suggest an evolutionary sequence for the origin of the different globin genes.
- *Use available evidence to assess the evidence that analysis of genes provides for evolutionary relationships:*
 - DNA sequencing has identifies similar genes in different organisms
 - **E.G.** The genes that code for the enzymes of respiration are very similar for every living organism, from bacteria to humans. This suggests that all organisms evolved from a single ancestor, and the gene for respiration first evolved in this common ancestor.
 - Also, the study of HOX genes provides evidence for evolution as the genes have remained similar for many organisms, and the function is the same regardless of what organism the gene is placed in.
 - The similarity of genes shows relatedness of organisms in relation to evolution, e.g. humans and chimpanzees share 98% of their DNA.