

Stem cells, gene expression and phenotype

Revision notes · Stem cells in medicine, differential gene expression, changes to mRNA after transcription, epigenetics, multiple alleles and polygenic inheritance.

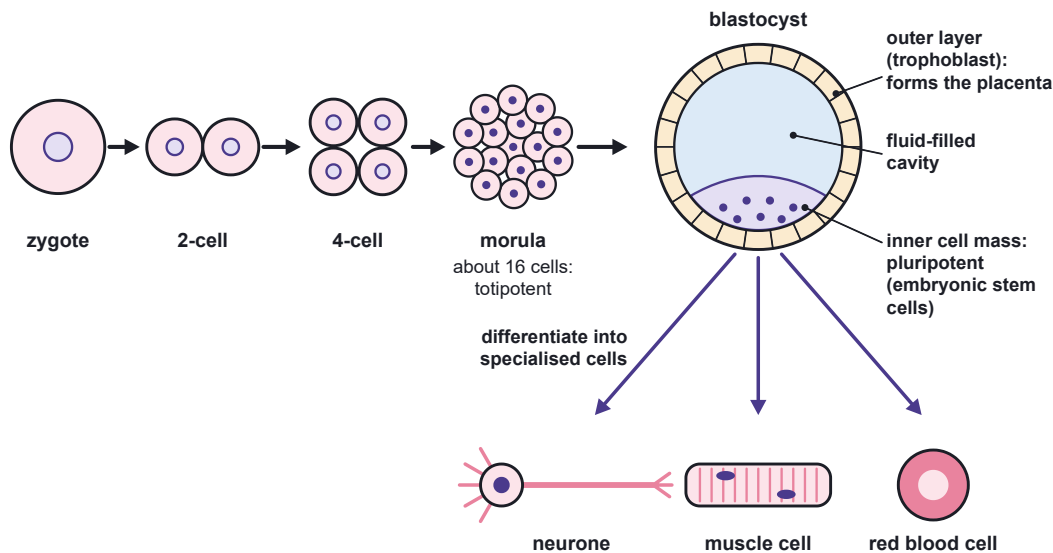
For Pearson Edexcel International AS Biology XBI11 and International A Level Biology YBI11. **A Level only** is IA2 content (Units 4 to 6), not needed for the International AS.

Stem cells, gene expression and phenotype **Spec 3.17-3.21**

Stem cells and potency **Spec 3.17**

Stem cell	An undifferentiated cell that can divide by mitosis to produce more stem cells and can differentiate into specialised cell types.
Totipotent	Able to differentiate into any type of cell, including the cells of the extra-embryonic tissues such as the placenta, so can form a complete organism.
Pluripotent	Able to differentiate into almost any type of cell in the body, but not extra-embryonic tissues, so cannot form a complete organism.
Morula	A solid ball of about 16 cells formed by early cell divisions (cleavage) of the zygote.
Blastocyst	A hollow ball of cells with a fluid-filled cavity, an outer layer of cells that forms the placenta, and an inner cell mass of pluripotent cells.

After fertilisation, the zygote divides repeatedly by mitosis, without growing, to form a **morula**. Its cells are **totipotent** at first. Further divisions produce a **blastocyst**: the outer layer (the trophoblast) forms the placenta and the inner cell mass becomes the embryo. The cells of the inner cell mass are **pluripotent**. They are known as embryonic stem cells and can be collected and grown in a culture to make specialised cells.



Morula cells are **totipotent**; cells of the inner cell mass are **pluripotent**.

Exam tip: The difference to remember: **totipotent cells can form any cell including the placenta (the whole organism)**; **pluripotent cells can form any body cell but not the placenta**.

Using stem cells in medical therapies Spec 3.17

Stem cells could be used to treat conditions in which cells are lost or damaged, such as some forms of blindness, spinal injury, Parkinson's disease and type 1 diabetes. Cells would be grown in culture, directed to differentiate, and transplanted into the patient. Bone marrow transplants, which use adult stem cells from bone marrow, are already used to treat some blood disorders. Adult stem cells avoid destroying an embryo, but they can form only a limited range of cell types.

Arguments about using embryonic stem cells	
For	Against
They could treat serious diseases and injuries that currently cannot be cured	Collecting embryonic stem cells destroys the embryo, which some people believe is a human life with the right to life
Spare embryos from IVF treatment would otherwise be destroyed	Some religious and moral views oppose any use of embryos; some people fear that it could lead to the creation of embryos for research
Stem cells divide indefinitely in culture, giving a large supply of cells	Risk of tumours if the cells divide uncontrollably after transplant, and of rejection or infection
Research gives scientific understanding of development and genetic disease	Treatments are expensive, and the benefits are still uncertain

Scientists provide evidence about what is possible and the risks involved, but they cannot decide whether the research should be done. Society makes the decision. Governments set laws and set up regulatory bodies that license and monitor research (for example, strict limits on how long embryos may be kept). Ethics committees, religious and patient groups, the media and the public all contribute opinions. Decisions can differ between countries and change as the science develops.

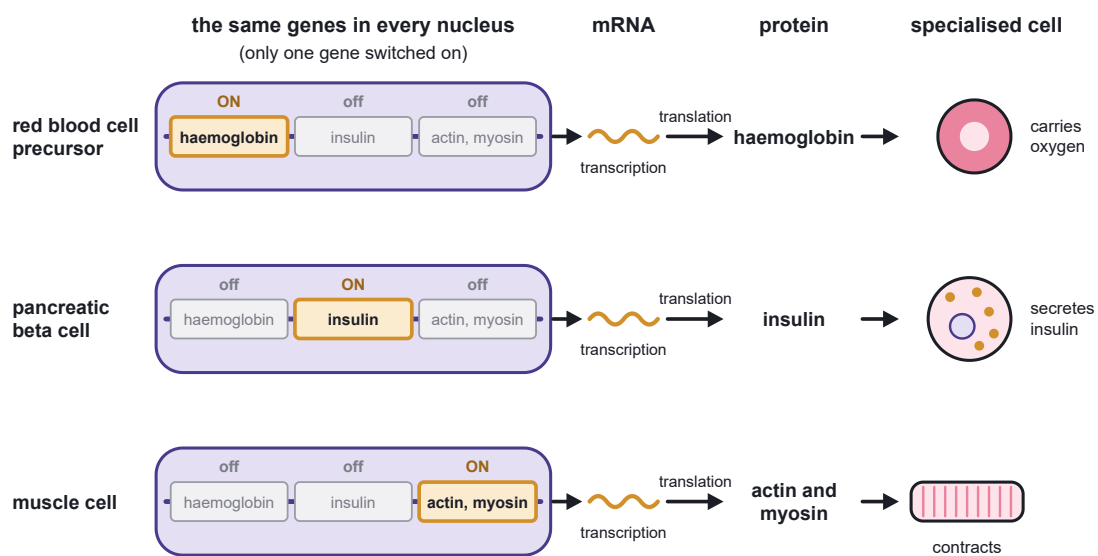
Exam tip: In a 'discuss' answer, give arguments on both sides (benefits and objections), and say who decides: laws and regulation, based on scientific evidence and public opinion.

Differential gene expression and specialisation Spec 3.18

Every body cell of an organism is produced by mitosis from the zygote, so each contains the same genome. Cells differ because of **differential gene expression**: in each type of cell, only particular genes are switched on and transcribed to **active mRNA**. The other genes in that cell are not transcribed.

1. Particular genes are switched on in a developing cell.
 2. These genes are transcribed to produce mRNA, which is processed into active mRNA.
 3. The mRNA is translated at ribosomes to give specific proteins.
 4. The proteins control cell processes (as enzymes) or determine cell structure, so the cell takes on its particular shape and function.
- **Animals:** in developing red blood cells the haemoglobin genes are expressed, so the cells fill with haemoglobin; in beta cells of the pancreas the insulin gene is expressed; in muscle cells the genes for contractile proteins (actin, myosin) are expressed.
 - **Plants:** in cells of the leaf, genes for photosynthetic proteins are expressed, whereas in root hair cells they are not; in xylem cells, genes are expressed for the enzymes that make lignin, which thickens the wall.

This is how a stem cell becomes a specialised cell: a particular set of genes is switched on, and the proteins they code for control the cell's structure and function. It is also why a cell can contain a gene that it never expresses.



Every cell has the same genes; **only some are switched on** in each cell type.

Common mistake: Specialised cells do not lose the other genes. They keep them all but do not transcribe them.

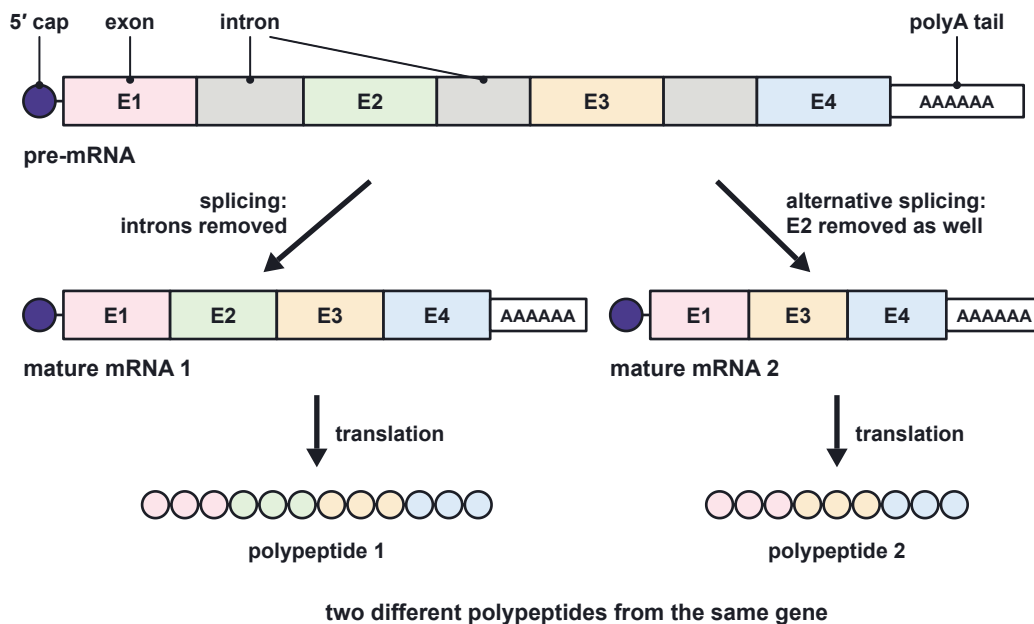
One gene, more than one protein Spec 3.19

The DNA of eukaryotic genes contains non-coding sections called **introns** between coding sections called **exons**. The whole gene is transcribed to give a primary transcript (pre-mRNA). Before it leaves the nucleus, it is changed. These are **post-transcriptional changes**.

1. The gene is transcribed to give pre-mRNA containing both exons and introns.
2. The introns are cut out and the exons are joined together. This is called **splicing**.
3. In alternative splicing, different combinations of exons are kept, or some exons are left out, so that different mature mRNA molecules are made from the same gene.

4. The mature mRNAs leave the nucleus through nuclear pores and are translated into different proteins (isoforms) with different amino acid sequences.

Alternative splicing means that the number of different proteins a cell can make is greater than the number of genes it contains. Different cell types may splice the same pre-mRNA in different ways, so the same gene can produce different forms of a protein in different tissues. Other changes to the pre-mRNA, such as adding a protective cap and a tail, also take place before the mRNA is used.



Alternative splicing: different combinations of exons give different proteins from one gene.

Exam tip: State that this is post-transcriptional (it happens after transcription, to the mRNA). Mutations change the DNA itself, so are different from splicing.

Genotype, environment and epigenetics Spec 3.20

The **phenotype** of an organism, its observable characteristics, is the result of an interaction between its **genotype** and the **environment**. Genes provide the potential, and the environment affects how it is expressed. Examples: height depends on genes and on nutrition; hydrangea flowers are pink or blue depending on the acidity of the soil; a plant grown in the dark has the genes for chlorophyll but is yellow; identical twins are genetically identical, but become different through different diets and lifestyles.

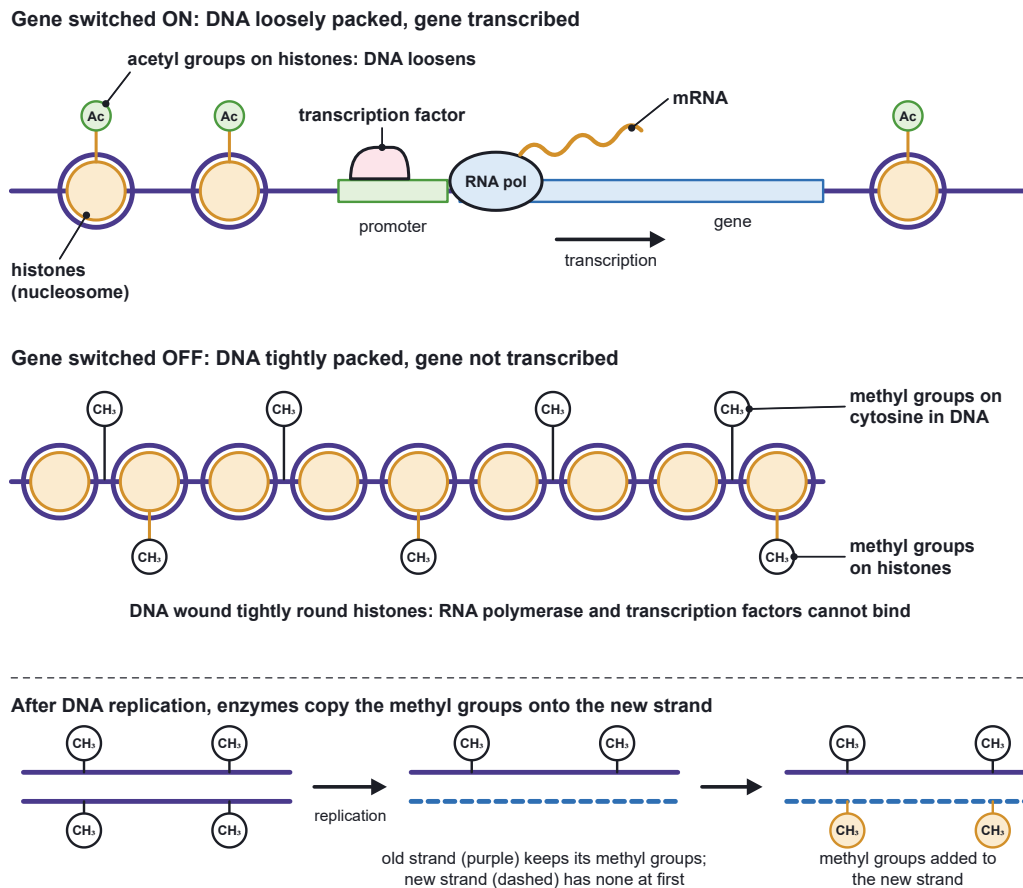
Epigenetic modification

Epigenetic modifications are chemical changes to DNA or to the histone proteins around which it is wound. They change whether a gene is **activated** (transcribed) without changing the sequence of bases.

- DNA methylation: methyl groups (CH_3) are added to cytosine bases in DNA. This usually stops transcription factors and RNA polymerase binding, so the gene is switched off (silenced).
- Histone modification: chemical groups are added to or removed from histones. Acetylation loosens the DNA from the histones, so the gene can be transcribed (activated). Deacetylation (and some kinds of histone methylation) makes the DNA wind more tightly, so the gene is not transcribed (switched off). Histone methylation can activate or repress a gene depending on where the methyl group is added.

The environment (for example diet, stress or smoking) can change the pattern of epigenetic marks. The epigenetic changes **can be passed on following cell division**: after DNA is replicated, enzymes copy the

methylation pattern onto the new strand, so daughter cells keep the same genes switched on or off. This is how a differentiated cell passes its pattern of gene expression on to its descendants.



Acetylation loosens DNA and switches genes on; **methylation** packs it tightly and switches genes off.

Exam tip: Epigenetic modification does not change the base sequence of DNA. Say that it changes gene activity (transcription), and that this is different from a mutation.

Multiple alleles, polygenic inheritance and variation Spec 3.21

Multiple alleles

An individual has only two alleles of a gene, but a gene can have more than two alleles in a population. The ABO blood group is an example. The gene has three alleles: I^A , I^B and I^O . I^A and I^B are codominant, and both are dominant to I^O .

ABO blood groups	
Genotype	Phenotype (blood group)
$I^A I^A$ or $I^A I^O$	A
$I^B I^B$ or $I^B I^O$	B
$I^A I^B$	AB
$I^O I^O$	O

A genetic cross with multiple alleles

A man of blood group A (genotype $I^A I^O$) and a woman of blood group B (genotype $I^B I^O$) have a child. Give the possible blood groups of the child.

1. Gametes of the man: I^A or I^O . Gametes of the woman: I^B or I^O .
2. Possible genotypes: $I^A I^B$, $I^A I^O$, $I^B I^O$, $I^O I^O$, in the ratio 1 : 1 : 1 : 1.
3. The phenotypes are AB, A, B and O.

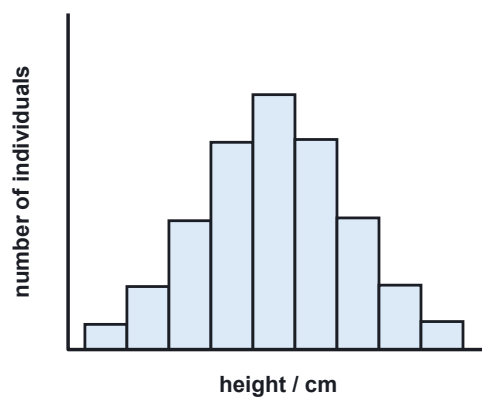
Answer: Any of the four groups A, B, AB or O, each with probability $\frac{1}{4}$

Polygenic inheritance and continuous variation

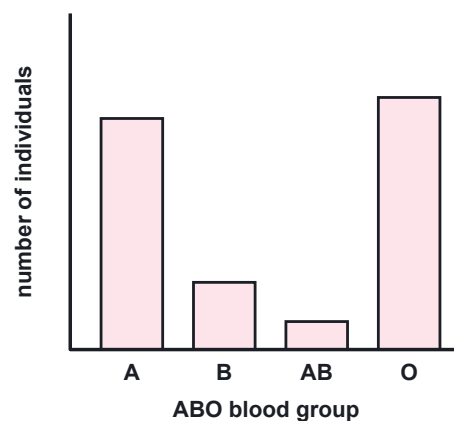
In **polygenic inheritance**, a characteristic is controlled by many genes at different loci, each contributing a small effect to the phenotype. These effects add together. Examples include human height and skin colour. The environment also affects the phenotype (for example, nutrition affects height). Together they give **continuous variation**: a range of phenotypes between two extremes, with no distinct categories. In a population the frequency distribution is usually a bell-shaped (normal) curve, and the characteristic is measured, not counted.

Discontinuous variation has distinct categories with no intermediates, such as ABO blood groups. It is controlled by one or a few genes and is little affected by the environment.

Maths skill: For continuous data, plot a histogram of the frequency table and find the mean (total $\div$ number), mode (most common value) and median (middle value when ranked). In a normal distribution these are about the same.



continuous variation
a range of phenotypes
between two extremes



discontinuous variation
a limited number of phenotypes
with no intermediates

Height shows **continuous variation** (polygenic, affected by the environment); blood group shows **discontinuous variation**.

Quick check

1. What is the difference between a totipotent cell and a pluripotent cell?
2. What is an exon?
3. How does DNA methylation affect gene expression?
4. Name the three alleles of the ABO blood group gene.
5. Why do cells with the same genes become different cell types?

Quick check answers

Stem cells, gene expression and phenotype

- 1 . A totipotent cell can form any cell type including placental cells; a pluripotent cell can form any body cell but not extra-embryonic tissue.
- 2 . A coding section of a gene, which is kept in the mature mRNA.
- 3 . It usually switches the gene off by preventing transcription.
- 4 . I^A , I^B and I^O .
- 5 . Different genes are expressed in each cell type, giving different active mRNA and proteins.