IB Biology HL: Mutations, Gene Editing, Reproduction & Water Potential

IB HL Study Guide

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Complete Study Guide

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Aligned to IB Biology HL 2025 syllabus — Theme D: Continuity and Change

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Section 1: Mutations and Gene Editing (D1.1, D1.2)

A **mutation** is a heritable change in the nucleotide sequence of DNA. Mutations are the ultimate source of all genetic variation. Without mutation, evolution could not occur — but mutations can also cause disease.

1.1 Types of Gene Mutations (Point Mutations)

Gene mutations (also called point mutations) affect individual nucleotides within a gene. There are two main categories:

Substitution mutations replace one nucleotide with another. Because the genetic code is degenerate (multiple codons encode the same amino acid), a substitution may or may not change the amino acid sequence:

MEMORISE THIS

Consequences of substitution mutations:

Type	Description	Example / Consequence
Silent (synonymous)	Base change does NOT alter the amino acid	UUU → UUC — both encode phenylalanine. No change in protein.
Missense	Base change alters ONE amino acid in the polypeptide	Sickle-cell anaemia: GAG → GUG changes glutamate to valine in haemoglobin
Nonsense	Base change creates a premature STOP codon	Polypeptide is truncated; usually non-functional

Insertion and deletion mutations add or remove one or more nucleotide bases. Because codons are read as triplets, adding or removing a base shifts the **reading frame** of all downstream codons — these are called **frameshift mutations**.

EXAM ALERT

Exam Alert — Frameshift mutations cause greater disruption than substitutions. A substitution alters at most one amino acid. A frameshift changes every codon downstream of the insertion/deletion, altering the entire C-terminal portion of the protein and often introducing a premature stop codon. When a question asks why an insertion is more harmful than a substitution, your answer must include the phrase **"reading frame shift."**

1.2 Chromosomal Mutations

Chromosomal mutations (also called chromosomal aberrations) affect the number or structure of entire chromosomes, not just single nucleotides.

MEMORISE THIS

Structural chromosomal mutations:

Type	Description	Consequence
Deletion	Segment of a chromosome is lost	Missing genes; often lethal if large
Duplication	Segment is repeated	Extra copies of genes; can lead to dosage effects
Inversion	Segment is reversed within the chromosome	Disrupts gene regulation; crossing over problems in meiosis
Translocation	Segment moves to a different (non-homologous) chromosome	Disrupts genes at breakpoints; may create fusion genes

Numerical chromosomal mutations (aneuploidy):

Failure of homologous chromosomes or sister chromatids to separate during meiosis (**non-disjunction**) produces gametes with incorrect chromosome numbers. If an aneuploid gamete is fertilised, the resulting zygote has an abnormal chromosome count.

Condition	Chromosomal change	Consequence
Trisomy 21 (Down syndrome)	Three copies of chromosome 21	Characteristic phenotype; learning differences; heart defects
Klinefelter syndrome (XXY)	Extra X in males	Infertility; reduced testosterone; tall stature
Turner syndrome (XO)	One X chromosome in females	Infertility; short stature; neck webbing

IB TIP

IB exam tip: Non-disjunction can occur in **meiosis I** (homologues fail to separate) or **meiosis II** (sister chromatids fail to separate). In both cases the result is aneuploid gametes. Questions may ask you to distinguish the meiotic stage at which non-disjunction occurred based on the gametes produced — this is a common HL mark-scheme target.

1.3 Mutagens

A **mutagen** is any agent that increases the rate of mutation above the spontaneous background rate.

MEMORISE THIS

Categories of mutagens:

Category	Examples	Mechanism
Physical	UV radiation, X-rays, gamma rays	UV causes thymine dimers (adjacent thymines bond covalently); ionising radiation breaks DNA strands
Chemical	Nitrous acid, benzene, aflatoxin	Deaminate, alkylate, or intercalate between bases, causing replication errors
Biological	Certain viruses (e.g. HPV, Hepatitis B)	Insert viral DNA near proto-oncogenes; disrupt normal cell-cycle control

The link between mutations and cancer: **proto-oncogenes** (genes that promote cell division) can become **oncogenes** through mutation, driving uncontrolled proliferation. **Tumour suppressor genes** (e.g. *p53*, *BRCA1*) normally halt damaged cells; loss-of-function mutations remove this brake.

1.4 CRISPR-Cas9 Gene Editing

CRISPR-Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats) is a precise gene-editing technology derived from a bacterial immune system.

Mechanism:

1. A **guide RNA (gRNA)** is designed to be complementary to the target DNA sequence (up to ~20 nucleotides).
2. The gRNA binds to the **Cas9 endonuclease** protein, forming a complex.
3. The gRNA-Cas9 complex scans the genome for the matching sequence and binds to it.
4. Cas9 cuts **both strands** of the DNA at the target site (double-strand break).
5. The cell's repair machinery then acts:
    - **Non-homologous end joining (NHEJ)** — error-prone; often introduces small insertions/deletions (indels) that disrupt the gene (**knockout**)
    - **Homology-directed repair (HDR)** — if a template DNA is supplied, the correct sequence is inserted (**knock-in**)

WORKED EXAMPLE

Worked Example: CRISPR mechanism steps

A scientist wants to correct the mutation in the *CFTR* gene that causes cystic fibrosis (a single-nucleotide deletion in exon 10, ΔF508).

(a) Describe the role of the guide RNA in CRISPR-Cas9 editing. [2]

(b) Explain which DNA repair pathway the scientist would want to exploit and why. [2]

Part (a) [2 marks]:

- The guide RNA is complementary to the target DNA sequence at the *CFTR* mutation site.
- It directs the Cas9 endonuclease to the correct location in the genome by base-pairing with the target sequence, enabling site-specific cutting.

Part (b) [2 marks]:

- The scientist would use **homology-directed repair (HDR)** by supplying a correct template containing the wild-type *CFTR* sequence.
- NHEJ is error-prone and would likely introduce further disruptive mutations rather than restoring the correct sequence; HDR uses the template to accurately replace the deleted nucleotide.

1.5 Gene Therapy

Gene therapy aims to treat or cure genetic diseases by introducing, altering, or replacing genetic material in a patient's cells.

MEMORISE THIS

Two approaches to gene therapy:

Approach	Description	Example
Somatic gene therapy	Target cells are non-reproductive body cells. Changes affect only the treated patient and are NOT heritable.	Treating sickle-cell anaemia by editing bone marrow stem cells
Germline gene therapy	Target cells are gametes or early embryos. Changes affect ALL cells of the resulting organism and ARE heritable.	Theoretically correcting a heritable mutation before implantation (currently banned in most countries)

Delivery methods (vectors):

- **Viral vectors** — modified retroviruses or adeno-associated viruses (AAV) that cannot replicate but insert therapeutic genes. Risk: insertional mutagenesis if the virus integrates near a proto-oncogene.
- **Non-viral methods** — liposomes (lipid nanoparticles), electroporation, or direct injection. Generally safer but less efficient.

⚠ EXAM ALERT

Exam Alert — Ethical considerations of gene editing. IB questions frequently ask you to "discuss ethical issues" surrounding CRISPR or gene therapy. You must present **both sides.** Potential benefits: curing heritable diseases, reducing suffering. Concerns: off-target edits, germline editing creating "designer babies," inequitable access, unintended ecological consequences if edited organisms are released. A balanced answer earns more marks than a one-sided list.

Section 2: Water Potential and Osmosis (D2.1)

Osmosis is the passive movement of water molecules across a partially permeable membrane from a region of **higher water potential** to a region of **lower water potential**.

2.1 Water Potential (Ψ)

Water potential (Ψ, psi) measures the tendency of water to move from one location to another. It is measured in **kilopascals (kPa)** and always has a value **less than or equal to zero** for biological solutions (pure water at atmospheric pressure = $\Psi = 0$).

The total water potential of a cell or solution is the sum of two components:

$$\Psi = \Psi_s + \Psi_p$$

MEMORISE THIS

Components of water potential:

Component	Symbol	Definition	Sign	Effect on Ψ
Solute potential (osmotic potential)	Ψ_s	Due to dissolved solutes; solutes reduce the free energy of water	Always negative (or zero for pure water)	Lowers Ψ
Pressure potential	Ψ_p	Due to physical pressure on the water	Positive in turgid plant cells (turgor pressure); can be negative (tension) in xylem	Raises Ψ if positive; lowers if negative

Key values to remember:

- Pure water: $\Psi = 0$ kPa

- A dilute solution: $\Psi < 0$ kPa (slightly negative)
- A concentrated solution: $\Psi \ll 0$ kPa (very negative)

Direction of osmosis: Water always moves from the region of **higher (less negative)** Ψ to the region of **lower (more negative)** Ψ.

2.2 Solute Potential (Ψ_s)

The solute potential depends on the **concentration of dissolved solutes**. As solute concentration increases, Ψ_s becomes more negative, which lowers the overall water potential and makes water less likely to leave (or more likely to enter).

For a simple ideal solution:

$$\Psi_s = -iCRT$$

where i is the ionisation factor (number of particles per formula unit), C is molar concentration (mol dm^{-3}), R is the ideal gas constant ($0.00831\ \text{dm}^3\ \text{MPa mol}^{-1}\ \text{K}^{-1}$), and T is temperature in Kelvin.

> **IB TIP**
>
> **IB exam tip:** You will not be required to calculate Ψ_s from the formula in most IB questions. However, you must know the relationship: **more solute = more negative Ψ_s = lower water potential = greater tendency to absorb water**. This logic underpins every osmosis question.

2.3 Pressure Potential (Ψ_p) and Turgor Pressure

In plant cells, the rigid **cellulose cell wall** resists expansion when water enters. As water enters by osmosis, the cell swells and the cell wall pushes back with a **wall pressure**. This inward pressure from the wall equals the **turgor pressure** pushing outward from within the cell.

- **Turgor pressure** is the positive Ψ_p that builds up inside a plant cell when it absorbs water.
- A fully **turgid** cell has maximum Ψ_p, and because Ψ_p is positive it partially offsets the negative Ψ_s, raising the cell's overall Ψ until eventually $\Psi_{\text{cell}} = \Psi_{\text{surroundings}}$ and net movement stops.
- A **flaccid** cell (lost water) has $\Psi_p = 0$; the cell's Ψ equals its Ψ_s (very negative).
- **Plasmolysis** occurs when a plant cell is placed in a hypertonic solution: water leaves so rapidly that the plasma membrane pulls away from the cell wall. The cell is said to be **plasmolysed**.

WORKED EXAMPLE

Worked Example: Calculating net water movement

A plant cell has $\Psi_s = -1200$ kPa and $\Psi_p = +400$ kPa.

It is placed in a solution with $\Psi = -600$ kPa.

(a) Calculate the water potential of the cell. [1]

(b) State the direction of net water movement. [1]

(c) Predict what will happen to Ψ_p as water moves. [2]

Part (a):

$$\Psi_{\text{cell}} = \Psi_s + \Psi_p = -1200 + 400 = -800 \text{ kPa}$$

Part (b): Water moves from the solution ($\Psi = -600$ kPa) INTO the cell ($\Psi = -800$ kPa) because the solution has higher (less negative) water potential.

Part (c): As water enters the cell, the cell swells and the cell wall exerts greater resistance. Ψ_p (turgor pressure) will **increase** (become more positive). This raises the cell's overall Ψ until equilibrium is reached when $\Psi_{\text{cell}} = \Psi_{\text{solution}}$.

2.4 Osmosis in Animal Cells

Animal cells have no cell wall, so they cannot develop turgor pressure. This makes them more sensitive to osmotic changes:

- **Hypotonic solution** (lower solute concentration than the cell): water enters → cell swells → may **lyse** (burst)
- **Isotonic solution** (same solute concentration as the cell): no net water movement → cell maintains normal volume
- **Hypertonic solution** (higher solute concentration than the cell): water leaves → cell **crenates** (shrinks and shrivels)

MEMORISE THIS

Comparison: osmosis in plant vs animal cells

	Plant cells	Animal cells
Cell wall present?	Yes (cellulose)	No
In hypotonic solution	Becomes turgid (wall prevents lysis)	Swells and lyses
In isotonic solution	Slightly flaccid (no turgor)	Normal
In hypertonic solution	Plasmolysed (membrane pulls from wall)	Crenated

⚠ EXAM ALERT

Exam Alert: Students often confuse the direction of osmosis with solute movement. Osmosis is the movement of **water** (not solute) across a membrane. Water moves toward the region of **lower** (more negative) water potential — that is, toward the more concentrated solution. Never describe solutes "pulling" water; describe water moving down its own potential gradient.

2.5 Experimental Determination of Water Potential

The water potential of plant tissue can be estimated by measuring changes in mass or length when tissue samples are placed in solutions of known concentration.

Procedure:

1. Cut uniform pieces of plant tissue (e.g. potato cylinders) and measure initial mass/length.
2. Place each piece in a series of solutions of different sucrose concentrations.
3. After a set time (e.g. 30 minutes), remove, blot dry, and measure final mass/length.
4. Calculate percentage change in mass for each concentration.
5. Plot % change in mass vs sucrose concentration.
6. The point where the graph crosses 0% change is the concentration at which $\Psi_{\text{solution}} = \Psi_{\text{tissue}}$.

IB TIP

IB exam tip: When asked to describe this experiment, always state you measure **percentage** change in mass (not absolute change), because initial masses of tissue pieces may vary slightly. Percentage change standardises the data. This is a 1-mark distinction examiners look for.

Section 3: Reproduction and Development (D3.1, D3.2)

Reproduction ensures the continuity of genetic information across generations. Sexual reproduction introduces genetic variation through meiosis and random fertilisation; asexual reproduction produces genetically identical offspring rapidly.

3.1 Sexual vs Asexual Reproduction

MEMORISE THIS

Feature	Sexual Reproduction	Asexual Reproduction
Gametes involved?	Yes — fusion of male and female gametes	No
Number of parents	Two (in most cases)	One
Genetic variation in offspring	High (meiosis + random fertilisation)	None (offspring are clones of parent)
Speed	Slower	Faster
Advantages	Variation aids adaptation to changing environments; variation reduces disease susceptibility	Energy-efficient; no need to find a mate; rapid population growth in stable environments
Disadvantages	Energetically costly; requires finding a mate	No variation — entire population vulnerable if environment changes or a pathogen evolves to target the genotype
Examples	Humans, flowering plants (via pollination)	Bacteria (binary fission), aphids (parthenogenesis), strawberries (runners/stolons)

3.2 Gametogenesis

Gametogenesis is the production of gametes (sex cells) through a series of mitotic and meiotic divisions. The meiosis-genetics guide covers the mechanics of meiosis itself; this section focuses on the biology of gametogenesis in animals.

3.2.1 Spermatogenesis (male gamete production)

Spermatogenesis occurs in the **seminiferous tubules** of the testes:

1. **Spermatogonia** (2n, stem cells in the germinal epithelium) divide by **mitosis** to maintain the stem cell population and produce primary spermatocytes.
2. **Primary spermatocytes** (2n) undergo **meiosis I** → two secondary spermatocytes (n).
3. **Secondary spermatocytes** (n) undergo **meiosis II** → four spermatids (n).
4. **Spermatids** undergo **spermiogenesis** (differentiation without cell division) → mature spermatozoa.

Each primary spermatocyte ultimately yields **four** functional spermatozoa.

Structure of a spermatozoon:

- **Head**: contains the haploid nucleus and is covered by the **acrosome** (a vesicle containing hydrolytic enzymes that digest the zona pellucida of the egg during fertilisation)
- **Midpiece**: packed with **mitochondria** to supply ATP for flagellar movement
- **Tail** (flagellum): propels the sperm

3.2.2 Oogenesis (female gamete production)

Oogenesis occurs in the **ovaries** and is distinctive because it is largely complete before birth:

1. **Oogonia** (2n) divide by mitosis and differentiate into **primary oocytes** during fetal development.
2. Primary oocytes begin **meiosis I** but arrest in prophase I. At birth, the ovaries contain all the primary oocytes a female will ever have (~1–2 million).
3. At puberty, each month one primary oocyte resumes meiosis I → secondary oocyte (n) + first polar body (discarded).
4. The **secondary oocyte** then begins **meiosis II** but arrests in **metaphase II**. This is the cell that is ovulated.
5. Meiosis II is completed **only if the secondary oocyte is fertilised** → mature ovum (n) + second polar body (discarded).

MEMORISE THIS

Key contrast: spermatogenesis vs oogenesis

Feature	Spermatogenesis	Oogenesis
Location	Seminiferous tubules (testes)	Ovaries
Functional gametes per precursor	4 spermatozoa	1 ovum (+ polar bodies)
Cytoplasm distribution	Equal (all cells similar size)	Unequal (one cell retains most cytoplasm — the oocyte)
Timing	Continuous from puberty	Begins in fetal life; arrests in prophase I; completes only on fertilisation
Arrest point	No arrest	Prophase I (fetus); Metaphase II (adult secondary oocyte awaiting fertilisation)

EXAM ALERT

Exam Alert — Meiosis II arrest. A very common exam question asks at what stage of meiosis the secondary oocyte is ovulated and what triggers completion of meiosis. The answer: the secondary oocyte is arrested at **metaphase II** and is ovulated in this state. Fertilisation by a sperm triggers completion of meiosis II and extrusion of the second polar body. Simply writing “the egg is released” without specifying the meiotic stage will lose marks.

3.3 Fertilisation and Early Embryonic Development

Fertilisation is the fusion of a haploid spermatozoon and a haploid secondary oocyte to form a diploid **zygote**.

Stages of fertilisation in humans:

1. The sperm penetrates the **corona radiata** (surrounding granulosa cells) and contacts the **zona pellucida** (glycoprotein coat of the egg).
2. The **acrosome reaction** occurs: the acrosome fuses with the sperm plasma membrane, releasing hydrolytic enzymes (acrosin, hyaluronidase) that digest the zona pellucida.
3. The sperm plasma membrane fuses with the oocyte plasma membrane. The sperm nucleus enters the oocyte.
4. Immediately, the **cortical reaction** occurs: cortical granules beneath the oocyte membrane fuse with it and release enzymes that harden the zona pellucida → **zona reaction** → **polyspermy block** (prevents more than one sperm fertilising the egg).
5. Penetration of the sperm triggers completion of **meiosis II** in the secondary oocyte.
6. The haploid nuclei of egg and sperm (**pronuclei**) fuse → **syngamy** → diploid zygote.

Early development:

Stage	Events
Cleavage	Rapid mitotic divisions of the zygote; cells (blastomeres) get smaller; no growth between divisions
Morula	Solid ball of ~16 cells
Blastocyst	Hollow ball; **inner cell mass** (ICM, embryoblast) will form the embryo; **trophoblast** will form the placenta
Implantation	Blastocyst embeds into the endometrium (~6–10 days after fertilisation)
Gastrulation	ICM reorganises into three **germ layers**: ectoderm, mesoderm, endoderm

> **IB TIP**
>
> **IB exam tip:** IB frequently asks about the significance of the **cortical reaction** and the **acrosome reaction**. Keep these distinct: the **acrosome** reaction allows sperm entry (enzymes digest zona pellucida); the **cortical** reaction prevents polyspermy (zona hardening after first sperm enters). Many students confuse the two.

3.4 In Vitro Fertilisation (IVF) HL

IVF (in vitro fertilisation) is an assisted reproductive technology in which eggs are fertilised outside the body.

Key steps:

1. **Ovarian stimulation:** The patient receives gonadotrophin injections (FSH and LH) to stimulate the development of multiple follicles simultaneously (superovulation).
2. **Egg retrieval:** Mature oocytes are aspirated from follicles using an ultrasound-guided needle.
3. **Fertilisation:** Sperm (from partner or donor) are incubated with the eggs in a culture dish. In ICSI (intracytoplasmic sperm injection), a single sperm is

injected directly into an oocyte.

4. **Embryo culture:** Fertilised eggs are cultured for 3–5 days (to blastocyst stage) in controlled conditions.
5. **Embryo transfer:** One or two viable embryos are transferred to the uterus. Remaining embryos may be frozen for future use.
6. **Luteal support:** Progesterone is given to support the endometrium for implantation.

⚠ EXAM ALERT

Exam Alert — IVF ethical considerations. IB Paper 3 questions frequently ask you to evaluate the ethics of IVF. Include: creation and potential disposal of surplus embryos, risks of multiple pregnancies, age limits for treatment, access (cost), use of donor gametes, preimplantation genetic diagnosis (PGD) and questions about "selecting" embryos. A balanced evaluation is always required.

Section 4: Gene Expression Regulation HL (D4.1, D4.2)

The DNA sequence (genotype) is not destiny — cells in the same organism share identical DNA yet have radically different structures and functions (a neuron vs a muscle cell vs a liver cell). This is because gene expression is tightly regulated. **Epigenetics** is the study of heritable changes in gene expression that do NOT involve changes to the DNA sequence itself.

4.1 Chromatin Structure and Gene Accessibility

DNA in eukaryotes is packaged around **histone** proteins to form **chromatin**. The fundamental unit of chromatin is the **nucleosome**: approximately 147 base pairs of DNA wound around an octamer of histone proteins (2 copies each of H2A, H2B, H3, and H4).

- **Euchromatin**: loosely packed chromatin. Genes in euchromatin are **accessible** to transcription factors and RNA polymerase → **transcriptionally active**.
- **Heterochromatin**: tightly packed chromatin. Genes are **inaccessible** → **silenced**.

The packaging state of chromatin is regulated by covalent modifications to **histone tails** — the flexible N-terminal extensions of histone proteins that protrude from the nucleosome.

4.2 Histone Modification

MEMORISE THIS

Key histone modifications and their effects on gene expression:

Modification	Enzyme(s) responsible	Effect on chromatin	Effect on transcription
Acetylation ($-COCH_3$ added to lysine)	Histone acetyltransferases (HATs)	Neutralises positive charge on histone; weakens DNA–histone interaction; loosens chromatin	**Activates** transcription (euchromatin)
Deacetylation (acetyl group removed)	Histone deacetylases (HDACs)	Restores positive charge; tightens DNA–histone interaction	**Represses** transcription (heterochromatin)
Methylation ($-CH_3$ added to lysine or arginine)	Histone methyltransferases	Effect depends on which residue is methylated	Can activate OR repress (context-dependent)
Phosphorylation ($-PO_4$ added to serine/threonine)	Kinases	Alters charge; affects higher-order folding	Varies; often associated with gene activation and chromosome condensation during mitosis

⚠ EXAM ALERT

Exam Alert: When writing about histone acetylation, the key mechanism is **charge neutralisation.** Histones are positively charged (lysine-rich). DNA is negatively charged. Acetylation removes the positive charge on lysine residues, weakening the electrostatic attraction between histone and DNA, allowing the chromatin to unwind and become accessible to transcription machinery. This molecular explanation distinguishes a 3-mark answer from a 1-mark answer.

4.3 DNA Methylation

DNA methylation is the addition of a methyl group ($-CH_3$) to a cytosine base, usually in the context of a **CpG dinucleotide** (cytosine followed by guanine in the 5'→3' direction). The enzyme responsible is **DNA methyltransferase (DNMT)**.

Effect on gene expression:

- Methylation of CpG sites in **gene promoter regions** generally **silences** gene expression.
- Heavily methylated promoters are associated with heterochromatin and reduced transcription factor binding.
- Conversely, **hypomethylation** of CpG islands (clusters of CpG sites) in promoters is associated with active transcription.

Inheritance of methylation patterns: DNA methylation patterns can be copied to the daughter strand after DNA replication by maintenance methyltransferases, which is

why they are described as **epigenetically heritable** — the pattern is transmitted to daughter cells.

MEMORISE THIS

DNA methylation vs histone modification — comparison:

Feature	DNA Methylation	Histone Modification
Target	Cytosine bases (CpG sites)	Histone tail residues (lysine, arginine, etc.)
Added group	Methyl ($-CH_3$)	Acetyl, methyl, phosphate, ubiquitin
Primary effect	Gene silencing (methylation of promoters)	Activation or repression (modification-dependent)
Heritability	Heritable — copied after replication	Can be heritable; less well characterised
Associated diseases	Cancers (aberrant methylation silences tumour suppressors)	Cancers, developmental disorders

4.4 miRNA Regulation of Gene Expression

MicroRNAs (miRNAs) are small (approximately 21–23 nucleotide) single-stranded RNA molecules that regulate gene expression **post-transcriptionally** — after the mRNA has been produced but before or during translation.

Mechanism:

1. miRNA genes are transcribed from the genome to produce **pre-miRNA** (a hairpin-loop precursor).
2. The pre-miRNA is processed in the nucleus and exported to the cytoplasm, where the enzyme **Dicer** cleaves it into a mature miRNA duplex.
3. One strand of the duplex is incorporated into the **RNA-induced silencing complex (RISC)**.
4. The miRNA within RISC base-pairs with the **3' UTR** (untranslated region) of its target mRNA.
    - **Perfect complementarity** → mRNA is **cleaved** and degraded.
    - **Partial complementarity** → translation is **blocked** (mRNA is not degraded but cannot be translated).
5. Result: the protein encoded by the target mRNA is not produced (or produced at reduced levels).

WORKED EXAMPLE

Worked Example: miRNA silencing

A researcher identifies a miRNA that targets the mRNA of a growth-promoting protein. When the miRNA is overexpressed in cells, proliferation decreases.

(a) Explain how the miRNA reduces production of the growth-promoting protein. [3]

(b) Suggest what might happen to cell proliferation if the gene encoding this miRNA were mutated and non-functional. [2]

Part (a) [3 marks]:

- The mature miRNA is incorporated into the RISC complex.
- The miRNA is complementary to a sequence in the **3' UTR** of the growth-promoting protein's mRNA.
- RISC binds the target mRNA, leading to either mRNA cleavage and degradation (if perfectly complementary) or blockage of ribosome activity / inhibition of translation (if partially complementary), preventing production of the growth-promoting protein.

Part (b) [2 marks]:

- If the miRNA is non-functional, the target mRNA would be translated at a higher rate (the post-transcriptional silencing mechanism would be lost).
- Increased production of the growth-promoting protein would stimulate cell proliferation, potentially contributing to uncontrolled cell growth/cancer.

4.5 Cell Differentiation and Epigenetic Reprogramming

All cells in a multicellular organism derive from a single zygote and have (with minor exceptions) the same genome. **Cell differentiation** is the process by which cells acquire specialised structures and functions through **differential gene expression** — different genes are expressed in different cell types.

How differentiation is established:

- During development, signalling molecules (**morphogens**, cell-surface signals, paracrine signals) activate transcription factors specific to each cell lineage.
- Once a cell fate is set, the epigenetic landscape (methylation patterns, histone modifications) is adjusted to stably silence genes not needed in that cell type and maintain expression of lineage-specific genes.
- This epigenetic state is inherited through subsequent cell divisions, creating stable cell lineages.

Epigenetic reprogramming can reverse differentiation:

- **Induced pluripotent stem cells (iPSCs):** Somatic cells can be reprogrammed back to a pluripotent state by introducing transcription factors (Oct4, Sox2, Klf4, c-Myc — the Yamanaka factors). This erases the cell-type-specific epigenetic marks and re-establishes a broadly permissive epigenome.

> **IB TIP**
>
> **IB exam tip:** A classic question asks why liver cells and muscle cells have different functions even though they have the same DNA. The correct answer at HL is: differential gene expression regulated by **epigenetic modifications** (histone acetylation/methylation and DNA methylation) and **transcription factors** determine which genes are actively transcribed in each cell type. "Different genes" is wrong — they have the same genes; they express different subsets.

> **MEMORISE THIS**
>
> **Summary: Levels of gene expression regulation**

Level	Mechanism	Examples
Chromatin / Epigenetic	Histone modification; DNA methylation	Acetylation opens chromatin; methylation of CpG islands silences genes
Transcriptional	Transcription factors bind promoters/enhancers	Activators increase RNA polymerase binding; repressors block it
Post-transcriptional	RNA processing, miRNA silencing	Alternative splicing produces different mRNAs from the same gene; miRNA blocks translation or degrades mRNA
Translational	Ribosome availability, initiation factors	Phosphorylation of eIF2 halts translation under stress
Post-translational	Protein modification, degradation	Phosphorylation activates/deactivates proteins; ubiquitin marks proteins for proteasomal degradation

Mixed Practice — Exam Style

10 MCQs covering all sections (IB Paper 1 style)

1. **[Mutations]** A single nucleotide insertion in the middle of a coding sequence most likely results in:

   A. A change in exactly one amino acid in the polypeptide

   B. A frameshift affecting all codons downstream of the insertion

   C. No change in the amino acid sequence because the code is degenerate

   D. Premature termination at the insertion site

2. **[Mutations]** Non-disjunction in meiosis I produces gametes with:

A. The correct number of chromosomes

B. Either two copies of one chromosome or no copies, in all resulting gametes

C. One extra nucleotide in the DNA sequence

D. A chromosomal translocation

3. **[CRISPR]** In CRISPR-Cas9 gene editing, what is the role of the guide RNA?

   A. It cleaves both strands of the target DNA

   B. It transcribes the replacement gene into mRNA

   C. It directs Cas9 to the correct DNA sequence by complementary base pairing

   D. It repairs the double-strand break by homology-directed repair

4. **[Water potential]** A cell has $\Psi_s = -900\ \text{kPa}$ and $\Psi_p = +300\ \text{kPa}$. Its water potential is:

   A. $-1200\ \text{kPa}$

   B. $+600\ \text{kPa}$

   C. $-600\ \text{kPa}$

   D. $-300\ \text{kPa}$

5. **[Water potential]** A plant cell is placed in a hypertonic solution. Which sequence correctly describes the changes?

   A. Water enters → cell swells → turgor pressure increases

   B. Water leaves → turgor pressure decreases → possible plasmolysis

   C. Solutes enter → cell shrinks → lysis

   D. No net movement occurs because the cell wall prevents osmosis

6. **[Reproduction]** The secondary oocyte is ovulated and remains arrested until:

   A. The LH surge at ovulation

   B. Penetration by a sperm triggers completion of meiosis II

   C. The oocyte reaches the uterus

   D. Progesterone levels fall after menstruation

7. **[Reproduction]** In spermatogenesis, one primary spermatocyte produces:

   A. One functional spermatozoon

B. Two spermatozoa and two polar bodies

C. Four functional spermatozoa

D. Two secondary spermatocytes that cannot divide further

8. **[Reproduction]** HL During IVF, multiple eggs are collected because:

   A. Each egg requires a different sperm donor

   B. Ovarian stimulation forces the ovary to release all stored primary oocytes

   C. FSH and LH injections cause superovulation, maturing multiple follicles simultaneously

   D. Each egg takes several weeks to mature in culture

9. **[Gene expression]** HL Histone acetylation promotes gene transcription primarily because:

   A. Acetyl groups directly activate RNA polymerase

   B. Acetylation reduces the positive charge on histones, weakening DNA–histone interactions and opening chromatin

   C. Acetylation methylates CpG islands in the promoter

   D. Acetyl groups bind to the TATA box and stabilise the transcription complex

10. **[Gene expression]** HL A miRNA with partial complementarity to a target mRNA will most likely:

    A. Cleave the mRNA at the base-pairing site

    B. Methylate the target gene's promoter

    C. Block translation by sterically hindering ribosome progression

    D. Increase transcription of the target gene

▶ Show Answers

May 2026 Prediction Questions

⚠ EXAM ALERT

These are NOT official IB questions. These are trend-based practice questions reflecting topic areas and question styles most likely to appear on the May 2026 IB Biology HL Paper 2. Based on recent exam patterns (2022—2025), expect significant weighting on: CRISPR and its ethical evaluation, water potential calculations, the secondary oocyte arrest and fertilisation sequence, and HL epigenetic mechanisms. CRISPR has appeared in IB papers for the first time in recent sessions and the topic is increasingly prominent.

WORKED EXAMPLE

Question 1 [Mutations and Gene Editing] [~9 marks]

A research group is using CRISPR-Cas9 to correct a missense mutation in the gene *HTT*, which causes Huntington's disease. The mutation is a single nucleotide substitution in exon 36 that introduces a premature stop codon, truncating the huntingtin protein.

(a) Distinguish between a missense mutation and a nonsense mutation. [2]

(b) Outline the mechanism by which CRISPR-Cas9 would be used to correct the mutation in somatic cells. Include the roles of the guide RNA and the Cas9 protein. [4]

(c) Evaluate the ethical considerations of using germline gene editing rather than somatic gene editing to treat Huntington's disease. [3]

▶ Show Solution

WORKED EXAMPLE

Question 2 [Water Potential] [~7 marks]

A student places five identical potato cylinders in sucrose solutions of different concentrations. After 30 minutes, the percentage change in mass of each cylinder is measured. The results are shown below.

Sucrose concentration (mol dm^{-3})	% change in mass
0.0	+8.2
0.2	+3.1
0.4	0.0
0.6	-4.5
0.8	-9.2

(a) Identify the water potential of the potato tissue. Explain your reasoning. [2]

(b) A cylinder in the $0.2\ \text{mol dm}^{-3}$ solution gained mass. Explain, using the concept of water potential, why water entered the cylinder. [3]

(c) Explain why the student measured percentage change in mass rather than absolute change in mass. [1]

(d) Predict the state of the potato cells in the $0.8\ \text{mol dm}^{-3}$ solution. [1]

▶ Show Solution

WORKED EXAMPLE

Question 3 [Reproduction and Gene Expression] [~8 marks]

(a) Describe the stages of oogenesis from oogonium to the point of ovulation, including the meiotic stage at which the oocyte is released. [4]

(b) HL Explain how histone acetylation and DNA methylation coordinate to control whether a gene involved in early embryonic development is expressed or silenced. [4]

▶ Show Solution