IB BIOLOGY | D1.3 | SL AND HL

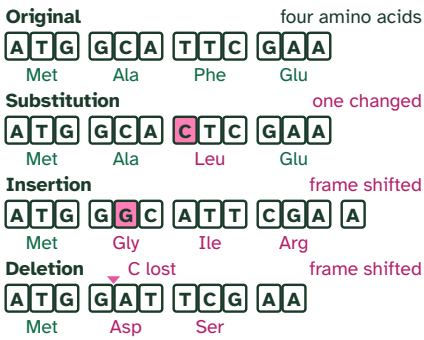
REVISION ON TWO PAGES

When a gene *changes*

What to know, what to draw and what to say. Nothing else.

THE ONE IDEA

A mutation changes the base sequence of a gene. What it does depends on what happens to the codons, and so to the polypeptide.



Read it in threes. One base swapped changes one codon; one base added or lost changes all that follow.

D1.3.1 START HERE

Three ways to *change* a gene

- A gene mutation is a **change to the base sequence** of a gene: a structural change to the DNA itself.
- **Substitution: one base swapped** for another. The gene keeps its length and at most one codon changes.
- **Insertion:** one or more **bases added**. **Deletion:** one or more **bases lost**. Both change the length of the gene.
- A ribosome reads in threes with nothing to mark where a codon ends, so an insertion or deletion can **change every codon after it**.

WHAT A SWAPPED BASE CAN DO

Same, Mistake, Stop

S **Same: silent**
new codon, same amino acid

M **Mistake: missense**
one amino acid different

S **Stop: nonsense**
a stop codon: chain cut short

D1.3.2

One base *swapped*

- The code is **degenerate**: most amino acids have several codons, usually differing only at the third base.
- So a substitution **may or may not change an amino acid**.
- A **single-nucleotide polymorphism** (SNP) is a base substitution found in some members of a population.
- **Missense is not always harmful:** it matters most in a key place, such as an active site.

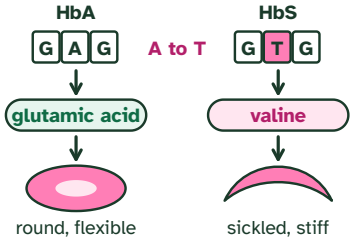
GGU to GGA silent
Both code for glycine: no change.

GAG to GAA silent too
Both code for glutamic acid: the sickle codon, unharmed.

D1.3.2 THE EXAMPLE

Sickle cell, one base

- In the sixth codon of beta globin, **A is replaced by T**: GAG becomes GTG.
- **Glutamic acid** (charged) becomes **valine** (non-polar): missense.
- At low oxygen haemoglobin S forms stiff fibres; cells sickle and **block small vessels**.
- Two copies of HbS give **sickle cell disease**.



D1.3.3

Bases *added or lost*

- Adding or losing one or two bases shifts the reading frame: a **frameshift**.
- Every codon after it can change and an **early stop codon** is likely (3 of the 64 codons are stops), so the polypeptide **almost never works**.
- A multiple of three keeps the frame, but whole amino acids are gained or lost.
- **Large insertions or deletions** usually stop a polypeptide working.

1 or 2 bases frame shifted
Every codon after it changes.

3 bases frame kept
One amino acid gained or lost.

D1.3.4

Where mutations *come from*

- **No outside cause:** rare **errors in DNA replication or repair** that proofreading misses.
- **Mutagens: chemicals** (benzo[a]pyrene and nitrosamines in tobacco smoke, aflatoxin from a mould, mustard gas) and **radiation**.

MUTAGENS

Smoke, Sun, Scans

S **Smoke**
chemicals in tobacco smoke

S **Sun**
ultraviolet: joins two neighbouring thymines

S **Scans**
ionising: X-rays, gamma rays, radon

D1.3.5

Mutation is *random*

- Mutation can happen **anywhere in the base sequence** of a genome.

1
Not equal odds
Some bases mutate more often, such as C beside G.

2
Not on demand
No known natural mechanism changes a chosen base for a trait.

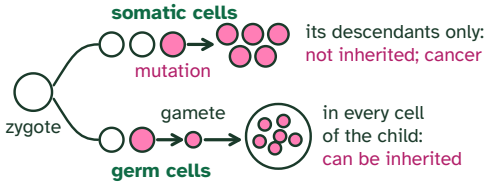
- Bacteria do not mutate to resist an antibiotic: **resistant mutants were already there**, and the drug kills the rest.

Who inherits a mutation, and how genes are *edited*

D1.3.6

Germ cells and somatic cells

- **Somatic cell:** only that cell's descendants carry it; it is **not inherited**.
- Somatic mutations in **genes that control cell division** can lead to **cancer**.
- **Germ cell:** via a gamete and zygote it reaches **every cell of the offspring**.



D1.3.7

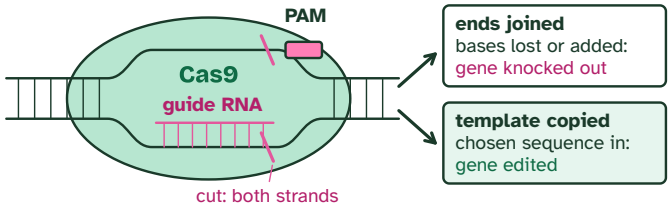
The source of all *variation*

- Every allele began as a mutation: the **original source of all genetic variation**.
- For one organism most mutations are **neutral or harmful**; for a species they are **essential for evolution** by natural selection.
- **Nature of science:** commercial genetic tests read SNPs and report disease risk. **Without expert interpretation** they can mislead: a raised risk is not a diagnosis.

D1.3.9 HIGHER LEVEL

CRISPR and Cas9: cut, then repair

- **Cas9**, an enzyme, carries a **guide RNA** of about 20 bases. Where the guide pairs, next to a **PAM**, it cuts both strands.
- The **cell's repair** makes the change: a knockout, or an edit copied from a template.
- **Success:** a patient's blood stem cells, edited to make **fetal haemoglobin**, treat sickle cell disease.
- **Nature of science:** some uses raise **ethical issues**; rules differ by country, so there is an effort to **harmonise** them.



D1.3.8 HIGHER LEVEL

Gene *knockout*

- A gene is made **inoperative**. How the organism differs from a **normal one** shows what the gene does.
- Model organisms: mice, zebrafish, yeast, *Arabidopsis*.
- **Libraries of knockout organisms**, one strain per gene, exist for some model species.

D1.3.10 HIGHER LEVEL

Conserved sequences: two hypotheses

- **Conserved:** the same or similar **across a species or group**; **highly conserved:** the same **over long periods of evolution**.
- **Function:** the product needs it, so **selection removes changes**; silent ones build up.
- **Slower mutation:** fewer changes arise at all, silent ones too.

	region X		region Y	
species A	GCT	AAG	TGG	CAT
species B	GCA	AAA	TGG	CAT
species C	GCC	AAG	TGG	CAT
species D	GCG	AAA	TGG	CAT
amino acid	Ala	Lys	Trp	His
	third bases vary		nothing varies	

WATCH OUT

Five mistakes that *cost marks*

- ✕ **A substitution changes at most one amino acid.** A frameshift can change all of them.
- ✕ **Mutations are not made on demand.** Selection acts on changes already there.
- ✕ **A somatic mutation is not inherited.** A smoker's lung cell does not make his sperm.
- ✕ **Cas9 only cuts.** The cell's repair makes the change; a near match can be cut by mistake.
- ✕ **Conserved does not mean unmutated.** Mutations arise there; selection removes them.

COVER THE SHEET

Can you *answer these?*

1. Distinguish substitutions, insertions and deletions.
2. Explain why a SNP may not change a polypeptide.
3. Describe the base and amino acid change in sickle cell.
4. Explain why losing one base is worse than losing three.
5. State two causes of mutation, and why it is random.
6. Compare germ cell and somatic cell mutations.
7. Outline how a knockout reveals what a gene does. HL
8. Explain how CRISPR-Cas9 can edit a gene. HL
9. Distinguish two hypotheses for conserved sequences. HL

IN THE EXAM

Follow the change down the chain: base, codon (or reading frame), amino acid, then the polypeptide's function. For sickle cell write both: **A to T**, and **glutamic acid to valine**.

GO FURTHER

Animated figures, a dry lab and a marked Check are in the full guide online.