

Mutations

Learning objective 6.7.A Describe the various types of mutation and explain how changes in genotype may result in changes in phenotype.

Name: _____

Date: _____

Period: _____

Use the tool **One Letter, Measured**. Parts 1 and 2 use **Every kind of mutation**, Parts 3 and 4 use **Where, and which base**, and Part 5 uses **Bigger changes**. You already know that a frameshift is worse than a substitution. The point of this worksheet is to find out **how much** worse, and why the answer is not the same for every frameshift.

Part 1 • The gene before anything happens to it

The gene is ATGGCATTACCAGGCTCTAAGGTTGACTGCTATGAAATTTGA. Transcribe it, then translate it, before you look at any mutation. You will need this protein as the standard everything else is compared with.

	Your answer
mRNA	
Codons	
Polypeptide	
Number of amino acids	

1. Define a mutation, and distinguish between a substitution and a frameshift.

Part 2 · Every kind of mutation, measured

Work through each mutation in the tool and record what it does. The last column is the number of the original protein's amino acids that do **not** survive.

Mutation	Bases altered	Protein length	Amino acids lost	% of protein
Wild type	0	13	0	0%
Silent substitution				
Missense substitution				
Nonsense substitution				
Insertion of 1 base				
Deletion of 1 base				
Deletion of 3 bases				

2. Using two figures from your table, explain why a frameshift is more damaging than a missense substitution even though both alter one base.

3. Deleting three bases does less damage than deleting one. Explain why, and state what that shows about which feature of a mutation actually determines the damage.

4. Explain why a silent mutation is possible at all.

Part 3 • The same mutation, in different places

Switch to **Where, and which base**. The identical single-base insertion is applied at each codon in turn. Record what it costs.

Insertion at codon	Amino acids lost	% of the protein	How much protein lies downstream
1			
4			
8			
12			

5. Explain why the same frameshift is more damaging near the start of a gene than near the end.

6. A student writes “a frameshift destroys the protein.” Rewrite that sentence so that it is accurate, using a figure from your table.

Part 4 · Which base of the codon was hit

The tool has tried every one of the **117** single-base substitutions possible in this gene's coding region. Record the breakdown by which base of the codon was changed.

Base of the codon	Silent	Missense	Nonsense	% silent
1				
2				
3				

7. A substitution occurs in the second base of a codon. State what will happen to the amino acid, and explain how you can be certain rather than merely likely.

8. Topic 6.4 measured the same pattern across the whole genetic code, before this gene was looked at. Explain why the agreement between the two calculations is worth more than either result on its own.

Part 5 · Bigger changes, and whether they are harmful

Use **Bigger changes, and whether they matter**. First the chromosomal mutations, then the two environments.

Type	What happens to the chromosome	Is any gene lost?	Can the phenotype change?
Duplication			
Deletion			
Inversion			
Translocation			
Nondisjunction			

9. Two of these can change a phenotype without any gene being lost. Identify them and explain how, referring to what Topic 6.5 showed about regulatory sequences.

10. Record the fitness of each genotype in each environment, then evaluate the statement “sickle cell is a harmful mutation.”

What the model simplifies

The gene is 42 bases long so that the whole of it, and the whole of its protein, fit on the screen at once. A real human gene is thousands of bases; the proportions destroyed by a frameshift are broadly similar but the absolute numbers are far larger.

Damage is counted as amino acids lost from the original sequence. A protein that keeps every amino acid may still be non-functional if a single change falls in the active site, and a protein that loses several may still work — so this count measures how much of the sequence survives, which is related to, but not the same as, whether the protein still does its job.

The gene has no introns, no regulatory sequences and no untranslated regions. Real mutations frequently land in those, and a mutation in a promoter or a splice site can abolish a protein entirely without changing a single codon.

Every possible substitution is treated as equally likely. Real mutation is biased: some base changes are commoner than others, and some sequences are far more mutable than the average.

The fitness figures for the two environments are illustrative rather than measured. The structure they demonstrate — that the sign of the heterozygote's advantage reverses between environments while the allele stays the same — is what the model is for, and that structure is well established for this allele.