AP BIOLOGY · UNIT 6 · TOPIC 6.7

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**. A frameshift is usually more damaging than a substitution. This handout measures **how much** more damaging it is, and why the damage is not the same for every frameshift.

Part 1 · The gene before anything happens to it

The gene is `ATGGCATTACCAGGCTCTAAGGTTGACTGCTATGAAATTTGA`. This is the coding (non-template) strand of the gene. Write the mRNA transcribed from this gene, then translate it, before looking at any mutation. Every mutation in Parts 2 to 4 is compared with this protein.

	Your answer
mRNA	
Codons	
Polypeptide	
Number of amino acids	

1. (a) Describe what a mutation is.

(b) Describe the difference between a substitution and a frameshift mutation.

Part 2 · Every kind of mutation, measured

Press each mutation button in turn, from Silent substitution to Deletion of 3 bases, and record what it does. The Amino acids lost 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 values from the Part 2 table, explain why a frameshift is more damaging than a missense substitution, even though both alter one base.

3. In the Part 2 table, deleting three bases does less damage than deleting one base.
(a) Explain why deleting three bases does less damage than deleting one base.

(b) Identify the feature of an insertion or deletion that determines how much damage it does.

4. Explain why a substitution can be silent.

Part 3 · The same mutation, in different places

Switch to **Where, and which base**. The same single-base insertion is applied at each codon in turn. Press Codon 1, Codon 4, Codon 8 and Codon 12, and record the damage at each.

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

5. Using the Part 3 table, explain why the same frameshift is more damaging near the start of a gene than near the end.

6. A student claims that “a frameshift destroys the protein.” Using values from the Part 3 table, evaluate the student’s claim.

Part 4 · Which base of the codon was hit

Stay on Where, and which base. 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 in this gene.
(a) Predict the effect of the substitution on the amino acid.

(b) Justify your prediction using the Part 4 table.

8. Topic 6.4 measured the same pattern across the whole genetic code, before this gene was examined. Explain why the agreement between the two sets of results is stronger evidence than either result alone.

Part 5 · Bigger changes, and whether they are harmful

Use **Bigger changes, and whether they matter**. Complete the table from the chromosomal mutations panel. Then press No malaria present and Malaria present in turn, and read the relative fitness of each genotype from the chart.

Type	What happens to the chromosome	Does the number of copies of any gene change?	Can the phenotype change?
Duplication			
Deletion			
Inversion			
Translocation			
Nondisjunction			

9. Two of the chromosomal mutations in the Part 5 table can change a phenotype without changing the number of copies of any gene.
(a) Identify the two mutations.

(b) Using what Topic 6.5 showed about regulatory sequences, explain how these mutations can change a phenotype.

10. The tool gives the relative fitness of three genotypes (HbA/HbA, HbA/HbS and HbS/HbS) in an environment without malaria and in an environment with malaria.
(a) Identify the genotype with the highest fitness in each environment.

(b) Using the fitness values, evaluate the claim that "the sickle cell allele, HbS, 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.