One Base Difference

Compare sequence records to investigate an inherited disorder.

GEN.5.7 "Enrichment: Use genomic databases for sequence analysis and apply the information to species comparisons, evolutionary relationships, and/or determine the molecular basis of inherited disorders."

NAME _____ DATE _____

1 READ AND MARK

Read it twice

YOUR JOB Underline the DNA triplets in the passage and circle the base that differs in the table. Number one piece of evidence about disease and one about shared ancestry.

A Clue in the HBB Gene

1. A search of the NCBI Gene database identifies HBB, the human gene that codes for beta-globin, a protein in hemoglobin. ClinVar lists rs334, a variant linked to sickle cell disease. Scientists compare such records by aligning DNA sequences so matching positions line up. The table focuses on one coding-DNA triplet at the same position in human, chimpanzee, and gorilla records.

ALIGNED HBB CODING-DNA TRIPLETS

Record	DNA triplet	Amino acid
Human, usual allele	GAG	Glutamate
Human, sickle allele	GTG	Valine
Chimpanzee	GAG	Glutamate
Gorilla	GAG	Glutamate

2. The usual human triplet is GAG, which codes for the amino acid glutamate. In the sickle allele, GTG codes for valine instead. This change affects beta-globin. When a person inherits two sickle alleles, the altered hemoglobin can clump under low-oxygen conditions, bending red blood cells and causing sickle cell disease. One sickle allele usually causes sickle cell trait, not the disease.

3. The chimpanzee and gorilla records have the same triplet as the usual human record. This agreement is consistent with that triplet being present in a shared ancestor. The sickle variant may have appeared later in the human lineage. One matching triplet cannot show which species are closest overall; scientists need many aligned positions across genomes to investigate that question.

2 ANSWER WITH EVIDENCE

Use the passage

1. Compare the two human records. Which DNA base changes, and at what position in the triplet?

2. How does that DNA difference change beta-globin, and how can two copies of the sickle allele cause disease?

3. Compare the usual human record with the chimpanzee and gorilla records. What idea about a shared ancestor does their match support?

4. A person has one GAG allele and one GTG allele at this position. What outcome does the passage suggest, and why?

3 YOUR TURN

Your own words

A different gene has a usual coding-DNA triplet of TTT (phenylalanine). A patient's record shows TCT (serine). Write a three-sentence database note identifying the base change, the protein change, and why this comparison alone cannot prove the variant causes disease.

ANSWER KEY

One Base Difference

PART 1 · READ AND MARK

Underline the DNA triplets in the passage and circle the base that differs in the table. Number one piece of evidence about disease and one about shared ancestry. Accept any marking that follows this job and points at the right text.

PART 2 · ANSWERS

#	QUESTION	ANSWER
1	Compare the two human records. Which DNA base changes, and at what position in the triplet?	**The second base changes from A in GAG to T in GTG.**
2	How does that DNA difference change beta-globin, and how can two copies of the sickle allele cause disease?	**Valine replaces glutamate in beta-globin. With two sickle alleles, altered hemoglobin can clump under low-oxygen conditions, bending red blood cells and causing sickle cell disease.**
3	Compare the usual human record with the chimpanzee and gorilla records. What idea about a shared ancestor does their match support?	**Their matching GAG triplets are consistent with GAG being present in a shared ancestor.**
4	A person has one GAG allele and one GTG allele at this position. What outcome does the passage suggest, and why?	**The person would usually have sickle cell trait, not sickle cell disease, because they have one sickle allele rather than two.**

PART 3 · YOUR TURN (SAMPLE ANSWER)

The patient's TCT differs from the usual TTT at the second base, where T changes to C. The new triplet codes for serine instead of phenylalanine, changing the protein sequence at this position. This comparison alone cannot prove the variant causes disease because clinical or functional evidence is also needed.

Accept answers that identify the second-base substitution and distinguish a sequence match from proof of ancestry or disease causation. For the patient with one sickle allele, accept that trait is the usual outcome.