Beyond the DNA

Investigating how genome tools inform gene therapy

BIO.3C.5 "Enrichment: Investigate current biotechnological applications in the study of the genome (e.g., transcriptome, proteome, individualized sequencing, and individualized gene therapy)."

NAME _____ DATE _____

1 READ AND MARK

Read it twice

YOUR JOB Underline what each technology measures, then number the places where the passage connects a measurement to a treatment decision. Use your marks to compare what the technologies can and cannot show.

Following the Evidence in Sickle Cell Disease

(1) A teenager with sickle cell disease has repeated pain episodes when some red blood cells become stiff and block tiny vessels. The condition often results from an inherited change in HBB, a gene that gives instructions for part of adult hemoglobin. A laboratory can sequence the teenager's DNA to identify the exact HBB variant, rather than infer it from symptoms alone. Sequencing reads the order of DNA bases, but it does not reveal which genes are active in a cell at a given moment. That matters because treatment decisions require more than a list of DNA changes.

(2) Researchers can study the transcriptome, the collection of RNA molecules made by cells, to see which genes are being used. They sample developing red blood cells because mature red blood cells have no nucleus and contain very little RNA. RNA measurements can show whether genes involved in fetal hemoglobin production are more active. A proteome study examines proteins instead: it can measure how much fetal hemoglobin the developing cells actually make. These tests answer different questions. More RNA does not always mean more protein, so both measurements help connect a DNA-based intervention to a possible change in the blood.

(3) One individualized gene therapy begins with a patient's blood-forming stem cells, which produce new red blood cells. Doctors collect the stem cells, use CRISPR to disrupt a DNA switch that normally helps suppress fetal hemoglobin in developing red cells, and return the edited cells after intensive preparation. This approach does not repair the HBB variant. It aims to raise fetal hemoglobin, which can reduce sickling. Teams can check DNA edits, RNA activity, and fetal hemoglobin protein levels, but the procedure carries serious risks and requires specialized care. Finding the intended DNA edit alone does not prove that treatment is safe or effective.

2 ANSWER WITH EVIDENCE

Use the passage

1. The teenager's pain episodes are already known. What additional information can individualized DNA sequencing provide, and why does that matter?

2. After editing, researchers find more RNA linked to fetal hemoglobin. Why should they also measure fetal hemoglobin protein?

3. Why does this therapy edit blood-forming stem cells instead of mature red blood cells?

4. Suppose a test finds the intended DNA edit, but the teenager still has pain episodes. Why is the DNA result alone not proof of treatment success?

3 YOUR TURN

Your own words

A fictional inherited disorder lowers an enzyme called K in skin cells. Researchers propose adding a working gene copy to those cells. In 4 to 5 sentences, design a before-and-after investigation using DNA sequencing, transcriptome analysis, and proteome analysis. State what each would measure and one reason the results might not prove the therapy is safe.

ANSWER KEY

Beyond the DNA

PART 1 · READ AND MARK

Underline what each technology measures, then number the places where the passage connects a measurement to a treatment decision. Use your marks to compare what the technologies can and cannot show. Accept any marking that follows this job and points at the right text.

PART 2 · ANSWERS

#	QUESTION	ANSWER
1	The teenager's pain episodes are already known. What additional information can individualized DNA sequencing provide, and why does that matter?	**It can identify the teenager's exact HBB variant rather than relying on symptoms to infer a DNA change.**
2	After editing, researchers find more RNA linked to fetal hemoglobin. Why should they also measure fetal hemoglobin protein?	**More RNA does not always mean more protein. Measuring the protein tests whether the cells actually make more fetal hemoglobin.**
3	Why does this therapy edit blood-forming stem cells instead of mature red blood cells?	**Stem cells produce new red blood cells. Mature red blood cells have no nucleus, so they are not suitable targets for this DNA edit.**
4	Suppose a test finds the intended DNA edit, but the teenager still has pain episodes. Why is the DNA result alone not proof of treatment success?	**The edit alone does not show that fetal hemoglobin increased enough to reduce sickling or that the treatment was safe.**

PART 3 · YOUR TURN (SAMPLE ANSWER)

Before treatment, I would sequence DNA from skin cells to identify the inherited change, then sequence treated cells to check for the added gene copy. I would compare enzyme K RNA in skin cells before and after treatment using transcriptome analysis. Proteome analysis would show whether the treated cells make more enzyme K protein. Together, these results could show that the added gene is present and being used. They would not prove the therapy is safe, because tests on sampled cells might miss harmful changes in other cells.

Accept responses that distinguish DNA sequence, RNA production, and protein production. For the open task, students should compare before-and-after measurements and name a plausible safety limitation.