

1. Researchers are investigating a rare metabolic disorder characterized by severe muscle weakness (myopathy) and high blood lactate levels even at rest. A biopsy of the patient's skeletal muscle revealed a mutation in the mitochondrial DNA (mtDNA) that encodes a subunit of Complex IV (Cytochrome c oxidase) in the Electron Transport System (ETS). Below is a table containing data from a patient with this disorder

**Data Table: Mitochondrial Analysis**

| Sample          | Oxygen Consumption ( $\mu\text{mol/min/mg}$ protein) | ATP Production (arbitrary unit) | Lactate Concentration (mmol/L) |
|-----------------|------------------------------------------------------|---------------------------------|--------------------------------|
| Healthy Control | 15.2                                                 | 100                             | 0.8                            |
| Patient         | 4.1                                                  | 25                              | 7.5                            |

You are invited by the team to analyse this data and propose molecular strategies to remedy the situation

**TASKS:**

- Account the relationship between Complex IV mutation, oxygen consumption, and ATP production shown in the data.
- Explain
  - Why the patient has elevated blood lactate levels even at rest
  - How the mutation leads to a faulty complex IV protein
- Propose a molecular biotechnology technique that could be used to identify the mutation

2. Recent oncology research at Ajanta pharmaceuticals highlights that many aggressive cancer cells exhibit the "**Warburg Effect**," where they prefer anaerobic fermentation over oxidative phosphorylation even in the presence of oxygen. Researchers measured the expression of a specific isoenzyme, **HK2 (Hexokinase 2)**, and the rate of lactate production in two cell lines: **Line A (Healthy Hepatocytes)** and **Line B (Hepatocellular Carcinoma)**.

| Cell Line | HK2 mRNA Levels (Relative) | Glucose Uptake ( $\mu\text{mol/min}$ ) | Lactate Produced ( $\mu\text{mol/min}$ ) | ATP Yield per Glucose |
|-----------|----------------------------|----------------------------------------|------------------------------------------|-----------------------|
| Line A    | 1.0                        | 5.2                                    | 0.8                                      | ~30-32                |
| Line B    | 14.5                       | 48.7                                   | 42.1                                     | ~2                    |

You are requested to analyse the data and explain them.

**TASK:**

- Analyse the relationship between HK2 protein synthesis and the metabolic shift observed in Line B.
- Explain
  - why a high rate of fermentation is advantageous to a rapidly dividing cancer cell, despite the significantly lower ATP yield per mole of glucose.
  - How the 30-32 ATPs are produced by line A cells
- If a clinician uses a CRISPR-Cas9 approach to knock out the promoter region of the HK2 gene in Line B, predict the impact on the Electron Transport Chain (ETC) activity and overall cellular pH. Justify your answer.

### ITEM 3

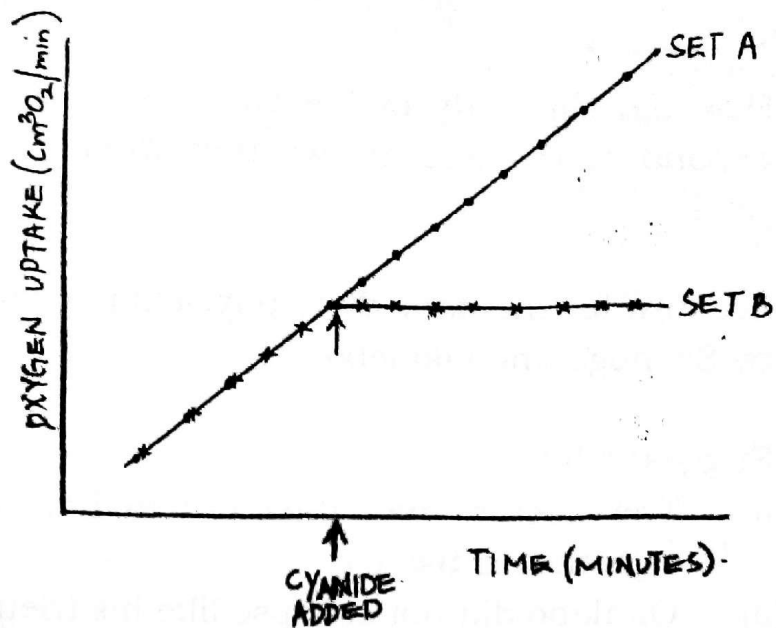
Doctor Lwanga is a sports biologist, studying a sprinter named Kiprotich. Kiprotich is a Ugandan gold medalist and is currently in high altitude training to improve his endurance. Dr. Lwanga takes a muscle biopsy (a small sample of tissue from Kiprotich's quadriceps before and after a four weeks training camp).

Upon analysis, Dr. Lwanga noticed that the post training muscle cells showed a 40% increase in the number of mitochondria, a denser network of rough Endoplasmic Reticulum (RER) and a significant higher concentrations of glycogen granules.

Furthermore, Doctor Lwanga isolates a specific gene that has been activated more frequently during this period that is gene coding for protein GLUT 4 which is responsible for transporting glucose into the cell.

#### TASKS.

- (a) Explain how changes in the membranous organelles support directly the cell's new functions during high intensity exercise.
- (b) Describe ,
  - (i) The journey of the GLUT 4 protein from the gene to the cell membrane.
  - (ii) How the gene provide information for the synthesis of GLUT 4 protein.
- (c) Explain how the higher concentration of glycogen granules enable Kiprotich to have more power for the exercise. (Detail of the mechanism of the Biochemical reaction may not be required).



### TASKS.

- Explain the observed differences in oxygen consumption between Set A and Set B on addition of cyanide. (05 scores)
- Explain the role of the following in cellular respiration.
  - cytochrome oxidase (03 scores)
  - oxygen (03 scores)
- Explain the likely effects of cyanide on the body cells of animals. (04 scores)

### ITEM 4

Ssenoga is thin and tall and his friend Okalebo has much hairs on his body, they both finished UACE in 2024. The two friends got an opportunity to visit a European country France for their long vacation. They were booked in a hotel. The following day, they stepped outside the hotel on a very cold, freezing, windy winter day without wearing a warm coat. While outside for a short time, they felt very cold and their bodies begun responding to the freezing weather, their skins developed a lot of goose bumps. Ssenoga particularly begun shivering and immediately collapsed. He was rushed to a nearby Hospital, while in the hospital, the doctors took long to see the veins on his arms to administer prescribed intravenous injection.

## TASKS

- (a) How did the body of the two best friends sensed and begun to respond to the freezing weather when they stepped outside their Hotel. (05 scores)
- (b) Account for the immediate physical physiological responses to cold by Ssenoga and Okalebo. (06 marks)
- (c) Suggest why,
- (i) The doctors had difficulty to immediately give intravenous injection to Ssenoga. (03 scores)
  - (ii) Okalebo did not collapse like his friend. (03 scores)
- (d) Advise Ssenoga and Okalebo on what they need to do, so that to manage the very cold weather during their vacation in France. (03 scores)

## ITEM 5

You are part of a team of neurobiologists and geneticists who are following this newly discovered tribe in amazon rain forest for a national geographical documentary. The people of this tribe are hunters in amazon forest, with many wild animals but many times they are alerted about such dangers by monkeys that produce specific sound signals and gestures and when they hear the call, they turn and look at the monkeys and immediately perceive the direction where the danger is and avoid it.

The tribe also uses a complex arrow poison called "Ixaya" for hunting. Some animals hit with ixaya-tipped arrows show immediate muscle paralysis and die while others enter a state of violent uncontrolled convulsions before death. Your team has isolated two key bioactive compounds from ixaya plant.

| BIOACTIVE MOLECULE | DESCRIPTION                                                                                                                                         |
|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|
| COMPOUND A         | A close analog of quabain, a chemical that disables the Na <sup>+</sup> -K <sup>+</sup> ATPase pump.                                                |
| COMPOUND B         | A novel neurotoxin that binds to the voltage gated sodium ion channels and prevent them from closing, effectively keeping them open once activated. |

Further, the team has discovered a rare genetic mutation in some rodent population in the same forest. The mutation was termed "The leaky barrier" as it severely reduces the function of potassium ion leak channels in neuronal membranes.

### TASKS.

- (a) Describe the basic pathways of flow of information through neurons that enable hunters hear and turn their neck to fully perceive the calls from the monkeys. (06 scores)
- (b) Explain the effect of treating neuron with compound A for a very long time on resting potential. (08 scores)
- (c) An animal with a leaky barrier mutation is hit with an ixaya tipped arrow. How would this pre-existing condition affect the resting potential. (04 scores)
- (d) Propose a coherent hypothesis that can explain the two different outcomes of the field trip. (07 scores)

## ITEM 6

Mr. Kei grows grapes in a green house where conditions are artificially modified, he ensures that there is always adequate carbon dioxide water, optimum temperature and light intensity, the light is provided by bulbs which run on electricity, he regularly tests the amount of sugars in his fruits, although for the past four days his electricity has been shutdown and it has greatly reduced the sugars in his fruits. His green house is near a dusty road, and the grapes in the side of the house close to the road have always showed even lower sugar content than others in the rest of the house, he noticed that their leaves have thick dust on them, he has suffered losses but he lacks a proper explanation for these changes in his grapes.

### Tasks:

- (a) Describe how the various adequate conditions maintained in the glass greenhouse promote synthesis of sugars in plants. (Details of the entire mechanisms may not be required) (12 scores)
- (b) As a student of plant nutrition assist Mr. Kei by explaining to him basically :
  - i) The effect of the electricity shutdown on his crops. (05 scores)
  - ii) The cause of the very low sugar content in the grapes near the road. (04 scores)
- (c) Give any benefits of glass greenhouse in farming. (04 scores)

END