1. A patient can perform nonstrenuous tasks but becomes fatigued upon physical exertion. Assays from muscle biopsy reveal that glycogen levels are slightly elevated relative to normal. Crude extracts from muscle are used to determine the activity of glycogen phosphorylase at various levels of calcium ion for the patient and for a normal person. The results of those assays are shown in the figure below. Briefly explain the findings.

![Response of glycogen phosphorylase to calcium ion in a patient and in a normal person](image)

2. A strain of mutant mice is characterized by limited ability to engage in prolonged exercise. After a high carbohydrate meal, these mice can exercise on a treadmill for only about 30 percent of the time a normal mouse can. At exhaustion, blood glucose levels in mutant mouse are quite low, and they increase only marginally after rest. When the liver glycogen in fed mutant mice is examined before exercise, the polymers have chains that are highly branched, with average branch lengths of about 10 glucose residues in either $\alpha$-1,4 or $\alpha$-1,6 linkage. Glycogen from exhausted normal mice has the same type of structure. Glycogen from exhausted mutant mice is still highly branched, but the polymer has an unusually large number of single glucose residues with $\alpha$-1,6 linkages. Practically all the chains with $\alpha$-1,4 linkages are still about 10 residues in length. Explain the metabolic and molecular observations for the mutant mice.

3. Vigorously contacting muscle often becomes anaerobic when the demand for oxygen exceeds the amount supplied through the circulation. Under such conditions, lactate may accumulate in muscle. Under anaerobic conditions a certain percentage of lactate can be converted to glycogen in muscle. One line of evidence for this synthesis involves the demonstration of activity for malic enzyme, which can use CO$_2$ to convert pyruvate to malate, using NADPH as an electron donor.

a. Why is lactate produced in muscle when the supply of oxygen is insufficient?
b. In muscle, pyruvate carboxylase activity is very low. How could malic enzyme activity facilitate the synthesis of glycogen from lactate?

c. Why would you expect the conversion of lactate to glycogen to occur only after vigorous muscle contraction ceases?

d. Is there an energetic advantage to converting lactate to glycogen in muscle rather than using the Cori cycle for sending the lactate to the liver, where it can be reconverted to glucose and then returned to muscle for glycogen synthesis?

4. Cyclic-AMP phosphodiesterase activity is inhibited by caffeine. What effect would drinking a strong cup of coffee have on glycogen metabolism in muscles when epinephrine levels are dropping in the blood?

5. An investigator has a sample of purified muscle phosphorylase \( b \) that she knows is relatively inactive.

   a. Suggest two methods \textit{in vitro} that could be used to generate active phosphorylase from the inactive phosphorylase \( b \).

   b. After the phosphorylase is activated, the investigator incubates the enzyme with a sample of unbranched glycogen in a buffered solution. She finds that no glycosyl residues are cleaved. What else is needed for the cleavage of glycosyl residues by active phosphorylase?

6. While muscle cells in tissue culture can be stimulated to break down glycogen only minimally when incubated in a solution containing cyclic-AMP, they are more readily stimulated by compounds like dibutyrylcyclic-AMP, whose structure is shown below. Explain the difference in response of cells to these two substances.

![Dibutyrylcyclic-AMP](image-url)