1. The [ATP]/[ADP] ratio varies during metabolic processes, however it is usually Kept high. For ATP hydrolysis reaction (ATP→ ADP + $P_i$) & using the bioenergetics equations you've taken in my lectures, please plot ΔG against lnX where X is the mass-reaction ratio (concentration of products over reactants) at 25°C & pH 7 for the concentrations of ATP, ADP, and $P_i$ in the following table. ΔG° for the reaction is –30.5 kJ/mol. According the plot generated, please provide a logical explanation for the high ratio of [ATP]/[ADP] in metabolism.

| Material | Concentration (mM) | | | | |
|---|---|---|---|---|---|
| ATP | 5.0 | 3.0 | 1.0 | 0.2 | 5.0 |
| ADP | 0.2 | 2.2 | 4.2 | 5.0 | 25.0 |
| $P_i$ | 10 | 12.1 | 14.1 | 14.9 | 10 |

2. Estimate the standard free energy for the following reaction & provide a logical explanation for your answer:

ATP + CDP → ADP + CTP

3. Technically, it is hard to determine directly the standard free energy change for ATP hydrolysis experimentally. This is because of the minute amount of ATP remaining at equilibrium, so measurements will not be accurate. It is calculated indirectly! Calculate the standard free energy change of ATP hydrolysis provided the following information:

Glucose 6-phosphate + $H_2O$ → glucose + $P_i$ K°eq = 270
ATP + glucose → ADP + glucose 6-phosphate K°eq = 890

4. As we studied before; metabolic pathways are either catabolic or anabolic. Nevertheless, there is a third type present in metabolism; it is called Amphibolic Pathway. These Amphibolic pathways can serve either in energy-yielding catabolic or in energy requiring (anabolic) biosynthetic processes; depending on the cellular circumstances. Based on this, do you consider the TCA cycle one of these pathways? Defend your answer.

5. There are many cases of human disease in which one or another enzyme activity is lacking due to genetic mutation. However, cases in which individuals lack one of the enzymes of the citric acid cycle are extremely rare. Why?

6. All the dehydrogenases of glycolysis and the citric acid cycle use $NAD^+$ as electron acceptor except succinate dehydrogenase, which uses covalently bound FAD. Suggest why FAD is a more appropriate electron acceptor than $NAD^+$ in the dehydrogenation of succinate.
(E° for $NAD^+$/NADH = -0.32 V)
(E° for FAD/$FADH_2$ in succinate dehydrogenase = 0.050 V)
(E° for fumarate/succinate = 0.031).

7. In electron transfer, only the cyclic quinone portion of ubiquinone undergoes oxidation-reduction; the isoprenoid (long hydrocarbon) side chain remains unchanged. Guess the function of this chain?

8. Isocitrate dehydrogenase is found only in the mitochondrion, but malate dehydrogenase is found in both the cytosol & mitochondrion. What is the role of cytosolic malate dehydrogenase?

9. Given that rotenone & antimycin A are equally effective in blocking their respective sites in the electron-transfer chain, which would be a more potent poison?

10. The relative degree of reduction of each carrier in the respiratory chain is determined by conditions in the mitochondrion. For each of the conditions below, predict the state of oxidation of ubiquinone, cytochrome *bc*1, cytochrome *c*, & cytochrome *c* oxidase.
    A. Abundant NADH, $O_2$ & cyanide
    B. Abundant NADH, but $O_2$ exhausted
    C. Abundant $O_2$, but NADH exhausted
    D. Abundant NADH & $O_2$

11. Electron transfer establishes a pH gradient across the inner mitochondrial membrane (IMM). Assume that during oxidative phosphorylation the mitochondrion is in a suspension medium of pH 7.4, the pH of the matrix has been measured as 7.7.
    A. Calculate [H+] in the inter-membranous space & the matrix under these conditions.
    B. What is the outside-to-inside ratio of $[H^+]$? Comment on the energy inherent in this concentration difference.
    C. Calculate the number of protons in a respiring liver mitochondrion (matrix); assuming the matrix is a sphere of diameter 1.5 mm.
    D. From these data, is the concentration gradient sufficient to generate ATP? Comment on how ATP gets generated thermodynamically.