TD 3 Metabolic regulation

Questions

1. **What is the main purpose of the citric acid cycle?**

To complete the oxidation of acetyl-CoA, producing $NADH$ and FADH for ATP generation in the electron transport chain, and to release carbon dioxide as a byproduct.

2. **Where does the citric acid cycle occur?**

In eukaryotic cells, it occurs in the mitochondrial matrix, with one enzyme succinate dehydrogenase located on the inner mitochondrial membrane. In prokaryotes, it happens in the cytosol because they lack mitochondria.

3. **What are the main inputs and outputs of one cycle turn?**

Inputs: Acetyl-CoA (from pyruvate), 3NAD^+, 1FAD^+ ,GDP, H_2O

Outputs: CO_2, 3NADH, 1FADH, GTP, COA-SH

4. **What is the relationship between the citric acid cycle and glycolysis?**

Glycolysis, the breakdown of glucose, produces pyruvate in the cytosol. Pyruvate is then converted to acetyl-CoA in the mitochondria, which is the entry point for the citric acid cycle.

5. **What are some key regulatory points of the citric acid cycle?**

Regulation occurs at three key enzymes: citrate synthase, isocitrate dehydrogenase, and alpha-ketoglutarate dehydrogenase. The pyruvate dehydrogenase complex, which generates acetyl-CoA, also acts as a critical gatekeeper and is regulated by the cell's energy status (ATP/ADP ratio) and product (acetyl-CoA).

6. **What are the primary regulatory points and mechanisms of the glycolysis pathway?**

The glycolysis pathway is regulated primarily at its three irreversible steps to meet the cell's energy demands (ATP production) and supply intermediates for other metabolic pathways. Regulation involves immediate allosteric control and covalent modifications (phosphorylation and dephosphorylation) control via hormones.

7. **In the table below , compare and contrast the effects of insulin and glucagon on the regulation of glycolysis in the liver. Focus on the enzymes involved in the regulation of fructose-2,6-bisphosphate levels.**

Insulin and glucagon exhibit reciprocal control over glycolysis in the liver, primarily by regulating the concentration of the potent allosteric effector **fructose-2,6-bisphosphate (F2,6BP)**. This regulation centers on a single, bifunctional enzyme that acts as both a kinase and a phosphatase

Features	Insulin (High Blood Glucose)	Glucagon (Low Blood Glucose)
Overall effect	Stimulates glycolysis	Inhibits glycolysis
F2, 6BP level	Increases F2, 6BP	Decreases F2, 6BP
Target enzyme	Bifunctional enzyme (PFK-2/FBPase-2)	Bifunctional enzyme (PFK-2/FBPase-2)
Enzyme activity	Promotes PFK-2 (kinase) activity	Promotes FBPase-2phosphatase) activity
Covalent modifications	Dephosphorylation of the PFK-2 enzyme (by phosphatse)	Phosphorylation of the FBPase-2phosphatase enzyme (by PKA)
Downstream effect	Activates PFK-1	Inhibits PFK-1

8. **What are the two main stages of oxidative phosphorylation?**

Electron Transport Chain

Electrons from NADH and $FADH_2$ are passed along a series of protein complexes, releasing energy that is used to pump protons (H^+) from the mitochondrial matrix to the intermembrane space.

Chemiosmosis

Protons flow back into the matrix through an enzyme called ATP synthase, and the energy from this flow drives the synthesis of ATP from ADP.

9. **What is the relationship between glycolysis, the citric acid cycle, and oxidative phosphorylation?**

Glycolysis and the citric acid cycle are the initial steps of cellular respiration that break down glucose, producing ATP and high-energy electron carriers, NADH and $FADH_2$.

Oxidative phosphorylation is the final stage where the energy stored in NADH and $FADH_2$ is used to produce a large amount of ATP.

10. **Illustrate the steps of oxidative phosphorylation mechanism or the electron transport chain**

The inner mitochondrial membrane contains four complexes II, III, IV, and I. Two mobile carriers presented by a small molecule named Coenzyme Q (Ubiquinone) between Complex I/II and III, and another small protein named Cytochrome c between Complex III and IV. An enzyme called ATP Synthase near Complex IV.

The steps to illustrate the process:

- ***Electron donation***

NADH (from the Krebs cycle and glycolysis in the matrix) releasing two high-energy electrons to Complex I, turning into NAD^+. $FADH_2$ (from the Krebs cycle in the matrix) releasing two electrons to complex II, turning into FAD. Complex II does not pump protons.

- ***Electron flow and proton pumping***

The electrons moving from complex I to coenzyme Q, then to Complex III, then to cytochrome c, and finally to complex IV.As electrons pass through complexes I, III, and IV, energy is released. This energy being used by these three complexes to actively transport **protons (H^+)** from the matrix into the intermembrane space.

- ***Water formation***

At the end of the chain (Complex IV), the electrons are transferred to the final electron acceptor is oxygen. The oxygen combines with these electrons and protons from the matrix to form water.

- ***Chemiosmosis***

Proton Gradient: Illustrate a much higher concentration of protons in the intermembrane space compared to the mitochondrial matrix. This is the electrochemical gradient or proton-motive force.

- ***ATP synthesis***

The protons flowing back into the matrix, down their concentration gradient, through the channel in ATP synthase. The ATP synthase used to combine ADP and inorganic phosphate to produce a large amount of ATP