



METABOLIC FATE OF PIRUVATE AND KREBS CYCLE

1. We are going to study a metabolic pathway involved in catabolism. For that, we are assembling a puzzle, which works like this: there will be available some clues about the metabolic pathway that we are studying and about the chemical structure of some compounds of that pathway. The goal of each group is to analyze and assemble all compounds in a logic sequence. For that, the group needs to schematize the pathway in the metabolic map, including all products and informations about reversibility of the reactions. You can use the “Study Mode” of the App ARMET Pathways to help you.
2. After assembling the pathway, indicate all involved enzymes.
3. After determining every enzyme and reaction, answer the questions in the App. For that, use the “Game Mode”. Finally, with the assistance of the textbook and your friends, discuss this study guide.

Clues:

- * Krebs Cycle starts with hydrolysis of coenzyme A of acetyl-CoA molecule. The next step consists of condensation of the Acetyl part with Oxaloacetate (OAA).
- * Eight enzymes participate in Krebs cycle reactions. Four of them present dehydrogenase action.
- * Every enzyme that presents dehydrogenase action needs of a coenzyme to work (NAD or FAD).
- * Only one of Krebs cycle enzymes uses FAD (Flavin Adenine Dinucleotide).
- * At the cycle's end, OAA is always regenerate, being produced two CO₂ molecules.
- * During Krebs cycle reactions an energy rich compound is produced (Succinyl-CoA).
- * The production of Citrate, α -ketoglutarate, and Succinyl-CoA involves irreversible reactions.
- * Decarboxylation of α -ketoglutarate is catalyzed by an enzymatic complex, similar to Piruvate Dehydrogenase complex. Such complex involves three enzymes and five coenzymes.
- * Krebs Cycle enzymes can be found only in mitochondrial matrix.
- * Krebs Cycle final products are: CO₂, NADH, FADH₂, GTP and H-SCoA.

Some enzyme types

Isomerases: Enzymes that catalyze isomerization reactions (change of chemical groups). Ex: Aconitase.

Dehydrogenases: Enzymes that catalyze hydrogen transfer reactions, i.e., oxi-reduction reactions, usually NAD or FAD. In mostly cases these reactions are reversible.

Synthetases: Enzymes that catalyze new molecules reactions by joining two existing molecules. This reaction needs energy to be done.

Fumarase: Enzyme that add a water molecule.

* The enzyme's name is related to the reaction that this enzyme catalyze. In many cases it is the name of the substrate or product of the reaction.



Questions

1. In the cellular metabolism, if there is enough oxygen, there is no reduction of Pyruvate to Lactate. In this case, Pyruvate can be transformed to Acetyl-CoA or Oxaloacetate. In other words, oxygen inhibits Lactate production but not ATP synthesis by Glucose breakdown. Why?
2. What are the fates of Pyruvate in an anaerobic reaction? Are they present in mammals?
3. Write the reaction of Acetyl-CoA production from Pyruvate and indicate:
 - a. Its cellular localization;
 - b. All 5 coenzymes and vitamins involved in this reaction.
4. Cite all Pyruvate Dehydrogenase inhibitors.
5. Write the reaction of Oxaloacetate formation from Pyruvate and indicate:
 - a. The enzyme which catalyzes this reaction;
 - b. The vitamin involved in this reaction;
 - c. The cellular localization of this reaction.
6. What is the role of Acetyl-CoA in regulating the activity of the enzymes Pyruvate Dehydrogenase and Pyruvate Carboxylase? Explain the physiological meaning of this regulation.
7. Analyze Coenzyme A structure and indicate which part of this molecule that binds to Acetate or Fatty Acid.
8. Compare coenzyme COA's role with the role of another coenzymes.
9. In Krebs cycle there is oxidation of an Acetyl-CoA molecule. So write the names of the compounds involved in this reaction and indicate the enzyme which catalyzes the reactions which there is production or consumption of:
 - a) CO_2
 - b) GTP
 - c) $\text{NADH} + \text{H}^+$
 - d) FADH_2
 - e) H_2O
10. Define what is substrate level phosphorylation and cite all Krebs cycle reactions related to this type of phosphorylation.
11. Which are the irreversible steps and the main regulation points of Krebs cycle?
12. Describe Pyruvate Carboxylase enzyme's role in the maintenance of Krebs cycle intermediates.
13. What is the importance of Anaplerotic reactions?
14. Cite the compounds that must be provided so Krebs Cycle could:
 - a) Start (and complete a round)
 - b) keep running
15. Cite Krebs cycle vitamins.
16. What is Krebs cycle cellular localization?
17. Cite Krebs cycle functions.



ARMET

Augmented Reality Metabolic Pathways
Realidade Aumentada Vias Metabólicas
Realidad Aumentada Vías Metabólicas

METABOLIC MAP (Assemble your pathway here)