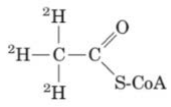
7.05 Spring 2020 Problem Set 11

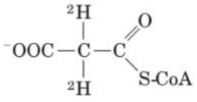
Problem 1: Fatty Acid Synthesis I

A) You are given a solution that contains all of the components necessary for fatty acid biosynthesis from acetyl-CoA and malonyl-CoA

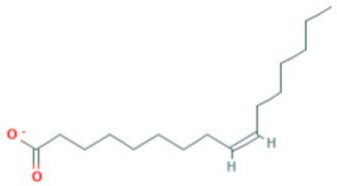
I) If [2-^{2}H]acetyl-CoA (deuterium labeled acetyl-CoA shown below) and an excess of unlabeled malonyl-CoA are used, how many deuterium atoms are incorporated into each molecule of palmitate and what are their locations?



II) If unlabeled acetyl-CoA and [2-^{2}H]malonyl-CoA are used, how many deuterium atoms are incorporated into each molecule of palmitate and what are their locations?



B) Palmitoleate is a common unsaturated fatty acid with a cis double bond at Δ_9.



Biosynthesis of Palmitoleate requires the use of palmitate as a precursor. Can this reaction be carried out in a completely anaerobic environment?

Problem 2: Fatty Acid Synthesis II

The acetyl group from acetyl-CoA in the mitochondrion is transported into the cytosol by a shuttle system in order to carry out fatty acid synthesis in the cytosol.

A) What is the name of this shuttle? Write the overall equation for the transfer of an acetyl group from the mitochondrion to the cytosol.

B) How many ATPs are needed in this process per acetyl group?

C) One result of the carnitine shuttle (facilitates β Oxidation) is the spatial separation of cytosolic and mitochondrial pools of acetyl-CoA. Does this acetyl group shuttle also accomplish this? Why is this important?

Problem 3: Pentose Phosphate Pathway

A) In mammals, mature red blood cells lack mitochondria and must instead rely on mitochondria-independent metabolic pathways. You observe that red blood cells generate both lactate and CO_2 as products of glucose catabolism. Describe the pathway(s) used by red blood cells to produce these.

B) It has been proposed that rather than operating sequentially (i.e. oxidative pentose phosphate pathway-followed by non-oxidative pentose phosphate pathway), it is possible for the pentose phosphate pathway to operate as a pentose phosphate cycle. Briefly explain how it would possible for products of the non-oxidative pentose phosphate pathway to re-enter the oxidative pentose phosphate pathway. Would such a cycle allow for the complete oxidation of glucose to CO_2 by red blood cells?

C) Red blood cells are continuously exposed to both endogenous and exogenous sources of reactive oxygen species like superoxide and hydrogen peroxide. What is one mechanism by which these ROS are neutralized? How might the increased use of the pathway described in **A)** allow red blood cells to better tolerate this oxidative stress?

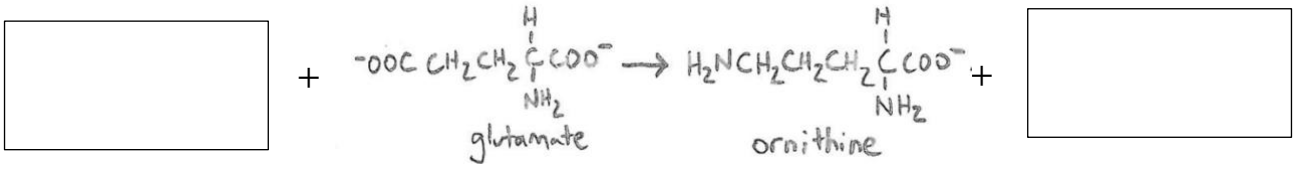
Problem 4: Nitrogen/Amino Acid Metabolism

A) Which steps of the urea cycle occur in the mitochondria and which occur in the cytosol?

B) Glutamine is the most abundant amino acid in the body. Why is glutamine so vital for survival? Include relevant reactions in your explanation.

C) When arginine is not available from the environment, cells use the same reactions as those found in the urea cycle to produce arginine. Describe how cells generate arginine from the amino acids ornithine and aspartate. Include all enzyme-catalyzed steps in your answer. It is not necessary to provide enzyme names or any reaction mechanisms, but for each step be sure to indicate all of the products and reactants. Assume ATP, CO_2 and NH_3 are freely available.

D) To net synthesize arginine, cells require a source of ornithine that is different from the production of ornithine in the urea cycle. Ornithine is generated via transamination, via the same PLP-dependent mechanism discussed in class. Glutamate acts as the primary amine donor. What are the other reactants and products for this process (draw the chemical structures).



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